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DIFFERENTIAL DIAGNOSIS OF RHEUMATIC FEVER IN OFFICE PRACTICE

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This discussion is based chiefly on experience gained in the examination of 2,639 children seen in consultation for the presence of active rheumatic fever and heart disease; it represents problems encountered by over 250 physicians in their practice. The errors in the early diagnosis of rheumatic fever and heart disease frequently result in labeling normal children rheumatic or cardiac. It is partly in hope of sparing some children needless invalidism that these observations are presented. The value of penicillin in the prevention of rheumatic fever also makes it important to accurately identify the rheumatic child so that he may be carefully maintained on long-term prophylaxis.

HEART MURMURS AND HEART SOUNDS

Systolic Murmur.—The finding which most often raises in the mind of the physician the question of the presence of rheumatic fever is the discovery of a systolic murmur. Eleven hundred fifty-one of the 2,639 children seen were referred for this reason. It is probably safe to say that every child, at some time in his life, has a functional or normal systolic murmur. The incidence of organic heart disease, both congenital and acquired, seldom runs over 1% in school children. When a systolic murmur is heard in a child the overwhelming probability is that it is not organic. The soft systolic murmur over the second left intercostal space, or so-called pulmonic area, is recognized by most physicians as a functional murmur. One far less common (although commoner in a diagnostic cardiac clinic) but far more often causing confusion is a murmur heard in the third left intercostal space with a musical, rasping, groaning, harsh, bleating, or sonorous quality, depending on the ear and imagination of the observer. This was called the "fiddle-string" murmur in the days when fiddles were in vogue. The murmur may be very loud and may transmit vibrations to the chest wall which resemble a thrill. It is short, extending only about two-thirds of the way through systole, and although it increases after exercise, as do almost all heart murmurs, it is usually considerably diminished in intensity in the erect position and is usually transmitted to the neck. The murmur of early mitral insufficiency, with which it may be confused, is never transmitted to the neck.

There are a number of other normal systolic murmurs, some heard between the apex and sternum and some at the apex. They are usually medium to low pitched, rather soft, and transmitted for only a short distance into the axilla after exercise with the patient in the left lateral position, and they usually diminish in the erect position. Because of their medium pitch they are filtered out by the diaphragm of the stethoscope or by pressing with the bell of the stethoscope (a maneuver of older clinicians which, in effect, makes a diaphragm of the underlying tensed skin). They are short, seldom extending more than two-thirds of the way through systole; they do not have the rather distinctive quality of the murmur of mitral insufficiency, nor are they transmitted far out into the axilla. Soft systolic murmurs over the aortic area occur in about 1% of children. They are transmitted to the neck, and in some cases it seems that the murmur actually originates in the neck and is transmitted to the aortic area. A child with such a murmur should be carefully investigated for congenital heart disease, although the great probability is that nothing will be found. Bilateral systolic murmurs under the clavicles can be caused by pressure of the scalenus anticus muscles on the subclavian arteries. Systolic murmurs can be heard and slight thrills can be felt over the vessels of the neck in the absence of any other finding suggesting heart disease. Rarely, two normal systolic murmurs can occur in the same heart. The presence of a well-defined normal systolic murmur should not exclude the search for a faint murmur of definite rheumatic heart disease.

Mitral Insufficiency.—The harsh, rasping, blowing murmur of a well-developed mitral insufficiency seldom causes confusion. It is the soft, early murmur which is often overlooked. It should be remembered that this murmur can be just as faint as the early murmur of aortic insufficiency. The quality of the murmur of mitral insufficiency can be reproduced by listening with the bell of the stethoscope on the back of the hand while the

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finger is passed over the adjacent skin with a light touch. It extends all the way through systole to the second sound (with one exception, which will be described below) and is transmitted far out into the axilla. It is best heard after exercise with the child lying in the left lateral position holding his breath in expiration; the diaphragm of the stethoscope should be placed briefly at the apex and then in the axilla. It should be emphasized again that normal systolic murmurs at the apex do not have the distinctive quality described, do not extend clear through systole, and are not transmitted far out into the axilla. The murmur of mitral insufficiency can be heard occasionally only as a late systolic murmur, and in these cases it may represent a healing mitral insufficiency. The murmur under these circumstances, although it starts late in systole, still extends clear to the second sound. This description applies only to the murmur of mitral insufficiency when active carditis is not present.

Adventitious Sounds.—There are a number of other normal findings on auscultation which may lead the examiner to suspect heart disease. One is a venous hum transmitted from the jugular veins of the neck to the precordium, especially when the child is looking to the left. It usually can be eliminated by compressing the veins of the neck, but occasionally it will persist, and in these cases it may be due to the flow of blood through deeper veins. It can be confused with a patent ductus arteriosus. Another fairly common finding is a systolic click. This sound is usually best heard between the apex and the sternum, shortly before the second sound, and is commoner in older children. There may be other adventitious sounds which are probably simply due to the rubbing of the heart on adjacent structures. It should be noted that passing the finger over the skin lightly does not produce a sound which can be heard with the unaided ear, although through the stethoscope it resembles the murmur of mitral insufficiency. Considering the position and activity of the heart, it seems extraordinary that it makes as little noise as it does. So-called cardiorespiratory murmurs should be classified with these sounds. These are adventitious sounds which vary with respiration. They are not common in children.

Heart Sounds.—The character of the first heart sound may raise some question in the mind of the examiner. It may be very loud; this is particularly common in thin-chested adolescent boys and is a normal finding. It may be markedly split to the point of reduplication. This is not an abnormal finding. When a loud first heart sound is present, however, the examiner should exercise the child and listen with great care for the presystolic murmur of mitral stenosis. Occasionally in a child with a very loud first heart sound a history of a low-pitched, apical middiastolic murmur will be obtained. Such children should be closely observed and classified as possibly having rheumatic heart disease. The second heart sound may be very loud normally. It is invariably split except in certain congenital defects. A third heart sound is present in 20 to 40% of normal children, depending on the ear of the observer. The normal third heart sound should not be confused with the protodiastolic gallop that occurs in a failing heart. Occasionally the third heart sound is slurred to a point where it resembles the middiastolic murmur of early mitral stenosis. Such children should be observed, but they usually turn out to have no heart disease, as do most children with questionable auscultatory findings. It should be emphasized, however, that any child who has unexplained dyspnea or limitation of exercise tolerance should have a careful cardiac investigation regardless of auscultatory findings. Ebstein's disease, constrictive pericarditis, endocardial fibroelastosis, tumors of the heart, aortic septal defect, and primary myocarditis are examples of conditions which are extremely rare and which can be overlooked.

Sounds in Congenital Heart Diseases.—Mention should be made of the forms of acyanotic congenital heart disease which are more commonly confused with rheumatic heart disease. These include coarctation of the aorta, patent ductus arteriosus, interventricular septal defect, mild isolated pulmonic stenosis, interauricular septal defect, congenital aortic stenosis, and subaortic stenosis. A murmur indistinguishable from the murmur of mitral insufficiency may occur at the apex in coarctation of the aorta. A middiastolic murmur may also occur. Careful blood pressure determinations in both arms and in the legs should always be made in the course of a cardiac evaluation, since the femoral pulses are often readily palpable in mild forms of coarctation and the blood pressure in both arms may be only slightly elevated or may be elevated only in the right arm. The flush technique is valuable in borderline cases. It should, however, be remembered that congenital mitral stenosis may accompany coarctation.

A rumbling middiastolic murmur is often heard at the apex in the presence of a patent ductus arteriosus; it disappears after operation. If a murmur resembling the murmur of mitral insufficiency is heard, the child should be carefully evaluated for the presence of rheumatic carditis before operation is performed. A harsh, relatively short systolic murmur in the second or third left intercostal space, with or without a thrill, suggests the diagnosis of interventricular septal defect, Eisenmenger complex, mild isolated valvular or infundibular pulmonic stenosis, or, more rarely, a patent ductus arteriosus, in which only a systolic murmur can be present in the school-aged child as well as in infancy. These lesions cannot be differentiated without special studies and sometimes not with them. Such murmurs should not be confused with the murmur of mitral insufficiency because of their location.

The criteria for precise clinical diagnosis of auricular septal defects in children are undergoing revision in the light of findings in surgically proved cases. A low-pitched middiastolic murmur within the apex and a high-pitched diastolic murmur along the left sternal border due to pulmonic insufficiency may occur with these lesions, suggesting mitral stenosis and aortic insufficiency. Fluoroscopic examination usually reveals evidence of a left-to-right shunt in these cases in the school-aged child. There are a number of congenital malformations which can be confused with the various forms of auricular septal defects, and even with special studies precise diagnosis is difficult. Aortic stenosis in the school-aged child without aortic insufficiency in the absence of mitral stenosis or insufficiency is very rare and, almost without excep-

tion, congenital in origin. Subaortic stenosis of both types is extremely rare and cannot be differentiated clinically from aortic stenosis or a high interventricular septal defect.

JOINT AND MUSCLE PAIN

Joint and muscle pain is the second commonest group of findings which raise the question of rheumatic fever in the mind of the examining physician. Five hundred fifty-three children were referred for this reason. Joint and muscle pains are extremely common in children. Examination of one unselected group of school children revealed that 20% at some time had had these complaints. Pains which are definitely not rheumatic are those which are present in the flexor muscles of the legs in the late afternoon or evening. They often awaken a child from sleep at night one or two hours after he has gone to bed. They are very common, but their cause is unknown. Joint and muscle pains are often caused by exertion and trauma following it. Children may forget these episodes unless carefully questioned. When the pains are in the legs, examination of the shoes may reveal that they do not fit properly. In the course of any acute and chronic infection, joint and muscle pains are common; these never should be confused with rheumatic fever.

Arthritis.—When rheumatic polyarthritis occurs following an acute upper respiratory tract infection, there is almost invariably a latent period between the acute infection and the onset of rheumatic manifestations. It should be remembered, too, that children who have been kept in bed for a week or two with a severe respiratory tract infection may complain of some pain in the legs the first few days after getting out of bed and walking. Joint swelling on the basis of allergy or drug sensitivity is not as painful as the polyarthritis of rheumatic fever, and usually all joints are affected simultaneously, in contrast with the migratory character of rheumatic polyarthritis. These children usually have swelling of the eyelids and may have urticaria (although urticaria can also accompany rheumatic fever). Rheumatoid arthritis is also not as painful as the polyarthritis of rheumatic fever and in the school-aged child is not common. The swelling is in proximal phalangeal joints and does not have the rapidly migratory character of rheumatic polyarthritis. Infectious arthritis in children is also uncommon, occurring only in 10 of the present series. In this instance, however, the polyarthritis may very closely resemble the polyarthritis of rheumatic fever. The pain is severe and may be migratory. It should be noted that in infectious arthritis, as in other infections and also in rheumatoid arthritis, slight prolongation of the P-R interval on the electrocardiogram may occur and a picture closely resembling acute rheumatic fever may result. Hospitalization and study are usually necessary in these cases.

Rheumatic Polyarthritis.—The pain in rheumatic polyarthritis is invariably severe. Although any joint may be affected, the wrists, elbows, shoulders, ankles, knees, and hips are most commonly involved. Although only one joint may be involved, this is very uncommon in children; two or more joints is the rule, and the pain moves from one joint to the other. The pain is worse on awakening in the morning. It is important when seeing children who are thought to have rheumatic polyarthritis not to administer salicylates immediately but to observe the child for the typical picture of migratory polyarthritis. Cortisone should not be used. Although rheumatic carditis can occur in the presence of a normal sedimentation rate, rheumatic polyarthritis is invariably accompanied by an elevated sedimentation rate. In evaluating fleeting joint pains in known rheumatic children, the physician should bear in mind the great frequency of these conditions in normal children and be cautious in interpreting them as signs of low-grade rheumatic activity.

ACTIVE RHEUMATIC CARDITIS AND ACTIVE RHEUMATIC STATE

One hundred sixty-nine children were referred for evaluation of the presence of the active rheumatic state or active carditis. This question is often raised in office practice when children have an upper respiratory tract infection which becomes chronic and long standing, with listlessness, pallor, fatigability, and vague muscle and joint pains, a picture which closely resembles low-grade rheumatic activity. In evaluating such children it is helpful to classify them into three groups.

1. The first group has a suppurative complication of an upper respiratory tract infection: sinusitis, tonsillitis, adenoiditis, or chronic bronchitis. They have low-grade fever, often sweat profusely, and complain of leg pain, usually worse in the afternoon; the sedimentation rate is slightly elevated. There are no signs of carditis. These children do not have rheumatic fever. Children with low-grade rheumatic fever do not sweat unless they are receiving salicylates, and when they have fever the sedimentation rate is almost always definitely elevated.

2. The second group has suffered from a hemolytic streptococcic infection or scarlet fever and thereafter has a persistent unexplained fever, elevated sedimentation rate, and fleeting joint pains and may also have conduction disturbances, as evidenced by slight prolongation of the P-R interval on the electrocardiogram and persistent tachycardia without alteration in rhythm, heart size, or heart sounds or development of a murmur. These children might be classified as having "poststreptococcic continuing disease." They are suffering from a sequel of streptococcic infection which is not suppurative. Such children should be closely observed for signs of active carditis and treated with rest and with careful attention to diet and general care, but they should not be labeled rheumatic unless the physician is convinced that carditis is present. Much needless alarming of parents could be saved by such a policy, although the physician may wish in his own mind to consider such children to be in the active rheumatic state. We doubt whether "poststreptococcic continuing disease" and rheumatic myocarditis are fundamentally the same disease process. The former definitely predisposes to the development of the latter, but it is our opinion, based on listening to many histories of the onset of carditis and on study of the disease in unselected school populations, that rheumatic myocarditis is precipitated by other episodes besides a streptococcic infection and can develop without a precipitating episode.

3. In the third group there may develop, in the course of rheumatic polyarthritis or as a sequel of an upper respiratory tract infection, scarlet fever, or a hemolytic streptococcic infection, one of several clinical syndromes indicating the presence of active carditis. A child with a previously normal heart may develop a diminished first heart sound with a poor, muffled quality; an accentuated second heart sound; and a third heart sound and appear clinically sick out of all proportion to the minimal clinical findings. Such a child may also develop, while under observation, a harsh, relatively short systolic murmur heard along the left sternal border, which sounds more like a murmur of congenital heart disease than a murmur of rheumatic heart disease. It resembles the murmur which is heard in complete heart block and is quite distinct from the murmur of mitral insufficiency. Later or concurrently the murmur of mitral insufficiency may develop. A soft, blowing diastolic murmur may appear along the left sternal border; this may persist for only a few days. A soft friction rub, without any electrocardiographic evidence of pericarditis, may also appear transiently without any other finding suggesting the presence of active carditis.

The onset of rheumatic carditis is often characterized by rapid development of the typical murmur of mitral insufficiency with a screeching quality accompanied by a brief middiastolic murmur, a first heart sound of poor quality, and an accentuated second heart sound. There is usually, although not invariably, a tachycardia. Such children should present no diagnostic problem. A child while under observation may develop a tachycardia in which there is an alteration in the relation of systole and diastole with lengthening of the former, giving a somewhat "tic tac" character to the rhythm. This is a definite manifestation of rheumatic myocarditis. Whether rheumatic myocarditis can be diagnosed in the presence of slight enlargement of the left ventricle alone, without auscultatory findings, is a question which cannot be answered on the basis of our experience.

Children with these evidences of early rheumatic myocarditis all appear clinically sick out of all proportion to the minimal physical findings. Fever, elevated sedimentation rate and antistreptolysin titer, cardiac enlargement, and an abnormal electrocardiogram are helpful but not essential confirmatory evidence. The diagnosis of active carditis can be made by auscultation regardless of laboratory findings. These variations of early low-grade carditis must often go unrecognized, since conservatively 40% of children with rheumatic heart disease found in the course of prevalence studies have no past history of a clinically recognized episode of rheumatic fever. If the physician is certain that an active carditis is present, cortisone therapy should be started in adequate doses.

FEVER OF UNKNOWN ORIGIN

Rheumatic fever is often considered when a child has an unexplained fever. One hundred seventeen children in the present series were referred for this reason. Careful attention should be given to the manner of taking the temperature. An oral two minute temperature reading of over 99.4 F should be checked by a rectal temperature reading. If this is under 100 F, fever is not present. There are children who normally have a temperature range higher than the accepted normal range and who will have fever just at the prospect of visiting a physician. In adolescent girls the fever may be preovulatory. Inquiry should be made concerning any recent immunizations, hypodermic medication, or drug ingestion. It should be remembered that dental apical abscesses ("gumboils") can cause slight fever. Careful blood studies, including the usual aggultinations, and especially careful investigation of the upper respiratory tract should be made. Mild hyperthyroidism should be considered; it was present in 22 of the present series. Although rheumatic fever can occur without fever, when fever is present the sedimentation rate is usually definitely elevated. A urinalysis should be done routinely in the differential diagnosis of rheumatic fever; it is occasionally necessary to examine several consecutive specimens in order to demonstrate pyuria.

NOSEBLEEDS

Because repeated nosebleeds are one of the manifestations of the rheumatic state, the possibility of the presence of rheumatic fever may be raised when a child has this sign. In this series 90 children were referred for this reason. Nosebleeds seldom occur as a manifestation of rheumatic fever unless other, unequivocal signs of rheumatic activity are present. Nosebleeds due to rheumatic fever are at first slight, usually occurring at night; they may later be profuse. Other causes to be considered are chronic upper respiratory tract infections, blood dyscrasias, and trauma. Some children have nosebleeds during hot weather, following exertion or trips to higher altitudes, and in the course of acute upper respiratory tract infections. Questioning may reveal that the tendency to nosebleeds is familial and there is no history of other rheumatic manifestations.

CHOREA

Fifty-four children were referred because of restless movements thought to be chorea. The pediatric cardiologist should form the habit of watching the extremities and, particularly, the muscles of the face while listening to the heart. Tics—rapid movements of a certain set of muscles at regular intervals—should be readily differentiated from chorea. Fine tremors should cause no confusion. Even very restless children can be persuaded to lie still for a minute (play Indian), while children with chorea cannot do this; slight involuntary movements will occur. The movements of chorea are performed by sets of muscles which would not contract together in the course of ordinary movements, even restless ones. Observing the child dressing and undressing, particularly in the course of tying and untying the shoes, may reveal the lack of coordination which accompanies early chorea. If a child is emotionally upset he should be examined with great care for this manifestation of rheumatic fever, because emotional instability is frequently the precursor of actual choreiform movements.

TACHYCARDIA

Forty-four children were referred primarily because of an unexplained tachycardia. The great majority of such cases are based simply on apprehension. It is always wise to have such children return for a second visit, and if possible a sleeping pulse should be obtained. With

extremely fast pulse rates paroxysmal tachycardia should be considered. The tachycardia of rheumatic carditis is often quite distinct from other forms of tachycardia, as has been noted. If the rate is unusually slow an electrocardiogram should be obtained, since heart block may be present. A peculiar, harsh systolic murmur which accompanies complete heart block may also lead one to suspect its presence when the rate is extremely slow.

OTHER SIGNS

Three hundred fourteen children were referred for various other reasons, chief of which were the presence of frequent colds or sore throats, unexplained elevation of the sedimentation rate, possible cardiac enlargement, and an abnormal electrocardiographic finding. The subject of respiratory tract infections has already been covered.

Elevated Sedimentation Rate.—The range of normal values of the sedimentation rate in children is wider than is usually given in textbooks, and children, for some unexplained reason, may have a slightly elevated sedimentation rate at the time of their first visit to the pediatric cardiologist, only to have a normal rate when they return. A diagnosis of rheumatic fever should never be made on the basis of one sedimentation rate or on the basis of the sedimentation rate alone. This procedure, when used in evaluating a child for the presence of rheumatic activity, should be very carefully and accurately done. Blood should be collected in tubes containing 0.1 mg. of heparin per cubic centimeter. It should be mixed by gentle inversion for three minutes and blood then withdrawn at once for the test, which should be performed within four hours of the time venipuncture is done. Tubes should be in the exact vertical position and should not be subject to extremes in temperature, and a hematocrit reading should always be obtained simultaneously. The Rourke-Erstene method is the method of first choice, with the Wintrobe method distinctly a second choice. The upper limit of normal values for the Rourke-Erstene method is 0.45 mm. per minute, corrected. Low-grade anemia is common in children referred for evaluation for the presence or absence of rheumatic fever, and, since it is the borderline rates which raise questions, a correction for hematocrit reading should always be made.

The presence or absence of rheumatic fever should always be evaluated on clinical grounds. Rheumatic fever can exist in the presence of a normal sedimentation rate. When, however, the sedimentation rate is elevated in the course of acute rheumatic fever, it is higher than in most acute infections which may be confused with it, while the white blood cell count is seldom elevated above 15,000 per cubic millimeter. The greatest value of the sedimentation rate determination is in evaluating the status of rheumatic fever which has already been diagnosed, since it is the last finding to return to normal. However, a child should not be kept in bed on the basis of a slightly elevated sedimentation rate alone. Far too much attention is paid to this procedure, and its results should never cause one to reverse one's clinical judgment. When the patient is an obese adolescent girl, it should be borne in mind that the sedimentation rate may normally be elevated. No relation of the sedimentation rate to menses has been noted. Poorly nourished children seem to have a borderline sedimentation rate more often than well nourished children. Finally, a few children seem to have an elevated sedimentation rate without any explanation; for them it is probably a normal finding.

Cardiac Enlargement.—Clinical evaluation of enlargement of the heart in children is inaccurate when checked routinely with fluoroscopic or roentgenographic findings. Usually, however, a point of maximal impulse more than 0.5 cm. outside the midclavicular line is an indication of an enlarged heart. An exception to this is in thin-chested children (usually boys) with an active, forceful heartbeat; in these cases the point of maximal impulse may well be outside the midclavicular line and the heart still be normal in size on fluoroscopy. The observer should take care not to confuse the impulse from the right ventricle in an enlarged heart with the point of maximal impulse and thus overlook the fact that enlargement is present. When a child is examined by fluoroscopy every effort should be made to gain his confidence because crying alters the contour of the heart. The great range of normality can only be appreciated by observing a large number of normal children. When the observer is in doubt about enlargement, it is probably not present. An absent or small aortic knob is normal in children, and a prominent pulmonary conus is also a very common normal finding. Localized bulging of the posterior contour in the left anterior oblique position usually indicates enlargement of the left ventricle, although this finding does not need to accompany the murmur of mitral insufficiency in order to establish the diagnosis. It should be noted that when enlargement of the left auricle is present it can almost invariably be seen in the left anterior oblique position as a slight bulging of the upper posterior contour before it is visualized in the right anterior oblique position with barium. Conversely, about 5% of children with otherwise normal hearts have definite slight indentation of the barium-filled esophagus in the region of the left auricle in the right anterior oblique position, with no sign of enlargement of this chamber in the left anterior oblique position and no other signs of heart disease.

It is questionable whether, in the absence of active rheumatic carditis, enlargement of the heart as a result of rheumatic fever occurs in the absence of the characteristic murmurs of rheumatic heart disease. There are children who have abnormally large hearts, with no other finding to indicate that heart disease is present. It is best to classify these cases as cardiac enlargement of undetermined cause.

Borderline Electrocardiogram.—As in fluoroscopic findings, only reading of a large number of electrocardiograms can give one a concept of the wide range of normality in children. The electrocardiogram is the procedure of least value in evaluating the presence or absence of rheumatic fever, because, when an abnormality caused by rheumatic fever is present, almost invariably other clear-cut rheumatic manifestations are present. Premature systoles are a fairly frequent and a normal finding in children. They do occur, however, as a manifestation of active rheumatic carditis and are more likely to be auricular or nodal in these cases. A marked sinus arrhythmia may be present and can be distinguished clinically by having the child hold his breath when the rate becomes regular.

It is well known that prolongation of the P-R interval often accompanies rheumatic fever, but this finding can occur normally without any other evidence of cardiac damage. As an isolated finding it should never be a basis for the diagnosis of rheumatic heart disease or active carditis. It can also occur in the course of other infections. We and others have found that the intramuscular injection of 1 mg. of atropine will cause the P-R interval to revert to within the limits of normality in these cases and also in cases in which the P-R interval is prolonged in the course of active rheumatic fever. This will not occur in children with prolonged P-R intervals resulting from repeated attacks of rheumatic carditis. Deviation of the ST segment beyond the usually accepted limits of normality is an occasional, isolated, unexplained finding. Precordial electrocardiograms rarely give information beyond that found on the standard limb leads as an aid to the differential diagnosis of rheumatic fever, although they are of value in following the course of active carditis.

COMMENT

The diagnosis of rheumatic fever and heart disease should be made with care. It is sometimes necessary to observe the child for weeks or months before a definite diagnosis can be made. Once it is established, however, the patient should receive year-round penicillin prophylaxis indefinitely and regardless of age. Although there is not unanimity among students of rheumatic fever concerning the exact nature of the relationship of streptococcic infection to the onset of a rheumatic episode, the existence of such a relationship seems unquestionable. Such patients should also receive early, intensive penicillin therapy for any respiratory tract infection. If hospitalized for rheumatic fever or any other reason, the child should receive penicillin prophylactically in some form. Prolonged cortisone therapy in doses sufficient to produce a definite Cushing effect should be given if the diagnosis of active carditis is made. We do not favor the use of cortisone for any other rheumatic manifestation than active carditis. It is of equal importance not to erroneously label a normal child rheumatic or cardiac. Until the observer is certain of the diagnosis, the child and the parents should be given the benefit of the doubt.

SUMMARY

Problems are encountered in office practice in the course of evaluating children for possible rheumatic fever or heart disease. The findings raising the question of the presence of rheumatic fever are, in order of frequency, (1) systolic murmurs, other murmurs, and abnormal heart sounds; (2) joint and muscle pains; (3) possible active rheumatic fever or carditis, especially as a sequel of an upper respiratory tract infection; (4) fever of unknown origin; (5) nosebleeds; (6) restless movements suggesting chorea; (7) unexplained tachycardia; (8) elevated sedimentation rate; (9) possible cardiac enlargement; and (10) questionable electrocardiographic findings. Conditions occurring in the normal child may be confused with signs of rheumatic fever.

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COMMUNITY CONTROL OF RHEUMATIC FEVER

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For several decades an obvious but not completely understood relationship has been recognized between beta hemolytic streptococcic infections and rheumatic fever.[1] This was well demonstrated with the advent of the sulfonamide drugs. It was found that when small daily doses of a sulfonamide were given to patients who had previously suffered attacks of rheumatic fever, repeated attacks of streptococcic sore throats were prevented and recurrences of rheumatic fever were rare.[2] Numerous studies[3] in attack rates of rheumatic fever in hospitals and clinics especially designed for the care of rheumatic children have shown the value of sulfonamides in this problem, so that it became almost a routine practice to give all children such prophylaxis after an attack of rheumatic fever, continuing this preventive measure through adolescence. More recent studies[4] have shown that buffered penicillin in small daily oral doses is an equally effective prophylactic agent.

Although of proven value, this type of prophylaxis was always started after the first attack of rheumatic fever. The abnormalities of the valves and myocardium, therefore, were already present before prophylaxis was begun. The prevention of the first attack, although of obvious importance, received less attention, because no practical method was known to accomplish it until the work of Rammelkamp and associates[5] showed that if streptococcic sore throats were adequately and quickly treated with penicillin the streptococci usually could be eradicated. It was shown that instead of the predictable 2.1% of their control (untreated) group in whom rheumatic fever developed, it developed in only a small per cent (0.25%) of the group treated for at least six days with penicillin. The tremendous practical importance of the work was immediately obvious. What heretofore had been an important but baffling problem, i. e.,

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3. Kuttner, A. G., and Reyersbach, G.: The Prevention of Streptococcal Upper Respiratory Infections and Rheumatic Recurrences in Rheumatic Children by the Prophylactic Use of Sulfanilamide, J. Clin. Invest. **22**: 77 (Jan.) 1943.

how to prevent first attacks of rheumatic fever, was partially solved, and all that was necessary to prevent the disease was to identify the patient with the streptococcic sore throat and see that adequate treatment with penicillin was given. This was done accurately and without too much difficulty in a military installation where the patients could not dictate their own treatment or follow-up. That it can be done in private practice was ably demonstrated by Breese with an amazingly large series, all proven by throat cultures and treated with a variety of penicillin preparations.[6]

The worrisome problem of detecting patients with streptococcic sore throats is not simply answered. Those patients with the typical fever, pharyngitis, exudate, and cervical adenopathy are sick, easily recognized, and usually get some medical attention, through which proper treatment can be started. However, the child with a streptococcic sore throat without the usual symptoms presents another problem. Rantz and his co-workers,[7] observing a large number of military personnel, produced convincing evidence that "a differentiation between streptococcic and non-streptococcic disease of the respiratory tract in adults may be made in northern United States with an accuracy of approximately seventy per cent without bacteriologic study of the throat flora, and in from eighty to ninety per cent if this laboratory procedure is included." This would imply that most patients in whom rheumatic fever develops would have a clinically detectable streptococcic sore throat one to three weeks previously. Of course, the knowledge and skill of the examiner are important here, but it is certain that rheumatic fever develops in some patients in whom it has not been preceded by the usual signs and symptoms of a streptococcic sore throat.

The public health implications of all this are obvious. A serious disease, responsible for a great deal of sickness, disability, economic loss, and death, can be prevented by an inexpensive drug, easily administered, if the patient can be detected. Prevention of a disease is especially important when the treatment is unsatisfactory. Despite early hopes and enthusiasm for corticotropin and cortisone in the treatment of acute rheumatic fever,[8] it appears that myocarditis and valvulitis often run the typical course even when the drugs are given over long periods of time and in large doses, and, at least in one carefully studied group, the results of treatment with these drugs were nearly identical to those seen in patients treated with aspirin.[9]

As rheumatic fever is a community problem, it seemed a challenge to the Youngstown Area Heart Association, and a program was undertaken in an effort to reduce the amount of rheumatic fever in this area and, in addition, to attempt to answer some of the questions that are implied by the preceding discussion.

PROGRAM

The program has several objectives, all centering around the prevention of first attacks of rheumatic fever. First, a countywide (Mahoning) educational program for school personnel, parents, nurses, and physicians about the importance of the detection of streptococcic sore throats and the necessity for correct treatment was started in 1950. This program has continued for the past five years, with some modifications each year. In addition to acquainting local physicians with the problem, it has consisted principally of talks by two Heart Association nurses, outlining the whole problem of the prevention of rheumatic fever to the principals, teachers, and school nurses in all 33 elementary and junior high schools in Youngstown. Similar sessions were held with the health chairman of each school's Parent-Teacher Association, followed by a letter to each chairman reemphasizing the importance of sore throat and the necessity and reasons for adequate penicillin therapy. Considerable literature relating to this problem was sent home with each school child in the city, in addition to a shorter, more specific note given to any child sent home because of a sore throat, explaining the reasons and importance of proper medical attention. Considerable newspaper and radio publicity about the purpose of the program has been given over this period, always emphasizing the necessity for adequate treatment of streptococcic sore throat.

Second, a program was started with a selected group of children, aimed at detecting streptococcic sore throats during the early phase of the disease by examinations and throat cultures and urging treatment of those children whose throat cultures were positive for beta hemolytic streptococci. The program with the school children, although still in progress, will be presented here in some detail, because it illustrates one approach to rheumatic fever prevention and some of the practical difficulties involved, and because it is hoped that the experience here with this program, despite some obvious imperfections, will aid and be a stimulus to others interested in community control of rheumatic fever.

In October, 1951, in order to establish practical procedures and techniques, a small group (100) of grade school children was chosen and this group steadily enlarged, so that during the school year 1952-1953, 1,017 students were followed in three different grade schools. The members of the county medical society were consulted and informed about the study, urged to take the diagnosis and treatment of sore throats seriously, and were reminded by mail of the proper treatment schedules. Parenthetically, it is our belief that no program of this

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6. Breese, B. B.: Treatment of Beta Hemolytic Streptococcic Infections in the Home: Relative Value of Available Methods, J. A. M. A. **152**: 10 (May 2) 1953.

7. Rantz, L. A.; Boisvert, P. J., and Spink, W. W.: Hemolytic Streptococcic and Nonstreptococcic Diseases of the Respiratory Tract, Arch. Int. Med. **78**: 369 (Oct.) 1946.

8. Hench, P. S.; Slocumb, C. H.; Polley, H. F., and Kendall, E. C.: Effect of Cortisone and Pituitary Adrenocorticotropic Hormone (ACTH) on Rheumatic Diseases, J. A. M. A. **144**: 1327 (Dec. 16) 1950. Massell, B. F., and Warren, J. E.: Effect of Pituitary Adrenocorticotropic Hormone on Rheumatic Fever and Rheumatic Carditis, ibid. **144**: 1335 (Dec. 16) 1950. Wilson, M. G., and Helper, H. N.: Effect of Pituitary Adrenocorticotropic Hormone (ACTH) in Acute Rheumatic Carditis, ibid. **145**: 133 (Jan. 20) 1951.

9. Houser, H. B.; Clark, E. J., and Stolzer, B. L.: Comparative Effects of Aspirin, ACTH and Cortisone on the Acute Course of Rheumatic Fever in Young Adult Males, Am. J. Med. **16**: 168 (Feb.) 1954.

type will be successful without first briefing the physicians of the county medical society on the need for the program and obtaining their promise of cooperation. Permission from the school board and promises of enthusiastic cooperation by school health physicians and nurses must be arranged before the program gets under way. The parents of all children involved were acquainted with the purpose of the program. This was done through talks to the Parent-Teacher Association, and a letter was sent to each home explaining in some detail the objects of the program and requesting parent cooperation.

Each morning, any child suspected by a teacher of not feeling well, or any child who had complained of any symptom suggesting sore throat, was sent to the Heart Association nurse, who had established an office in the selected schools. She carefully examined the child's throat and neck and took the child's temperature. Throat cultures were taken if the child had a red throat, complained of a sore throat, or had significant cervical lymphadenopathy. If there was any question as to whether the throat was sore or abnormally red, a throat culture was taken. If the child had a red throat or fever, he was sent home with a note stating that a throat culture had been taken and giving a reminder of the importance of the recognition and treatment of streptococcic sore throat. A complete list of absentees was made each morning, and, if the reason for absence was not known, a telephone call was made to the child's home. If the child had a sore throat or a temperature of 102 F or higher, the nurse visited the home and the procedure described at school was carried out. These cultures were taken to the Youngstown Hospital laboratory that day and were reported by the next morning as negative or positive for beta hemolytic streptococci. If positive, the child's family was immediately contacted, given the information, and urged to consult the family physician. The physician was contacted, told of the positive culture, and reminded of the Heart Association program and the necessity for adequate penicillin therapy. The mother was again contacted the following day, and, if no action had been taken, was again urged to see the family physician. All children with positive cultures were watched rather carefully for several weeks after returning to school. During the latter part of the study all children returning to school had repeat throat cultures.

RESULTS

Of the 1,017 children followed, 650 had one or more throat cultures taken, for a total of 872 cultures, 52 (6%) were positive for beta hemolytic streptococci. Twenty-four of these cultures (46%) were taken at home, and 28 (54%) were taken at school. Of the 52 children with positive cultures, 46 (88%) complained of a sore throat, 38 (73%) had red throats on inspection, 39 (75%) had a temperature of less than 100 F, and 13 (25%) had a temperature of 100 F or higher. Of the 52 children with positive throat cultures, only 15 (29%) received what was felt to be ideal treatment (six to eight days of penicillin therapy, with adequate daily dose); 27 (52%) received some treatment with penicillin, but not for six to eight days or not in an adequate daily amount. In this group, however, 23 of the 27 had repeat throat cultures on returning to school, and 18 (35% of the 52) were found to be negative, and so these children might be considered to have had "adequate" therapy; 10 (18%) received no therapy. The usual reason for inadequate therapy was the reluctance of the parent or the physician to start or continue treatment in the absence of severe symptoms. Rheumatic fever did not develop in any of the children in the group studied.

COMMENT

The low percentage of positive cultures is due to the large number of cultures taken in children who had only mild or moderate sore throats, or children with high grade fever and moderate sore throats who later proved to have other infectious diseases, such as measles, influenza, or other viral diseases. Of the 52 children with positive cultures, it was not definitely known which had streptococcic infections and which were streptococcic carriers, except for one person with typical scarlet fever and one with acute otitis media. Certainly some of the children with only mild pharyngitis and no fever were only streptococcic carriers. No antistreptolysin titers were performed, and in distinguishing between streptococcic sore throat with a few signs and symptoms as opposed to a viral upper respiratory infection with coincidental positive cultures, no absolute distinction could be made. It was felt better to overtreat than to undertreat, and so therapy was urged for all children with a positive throat culture. It was particularly difficult to see that children with mild symptoms got adequate treatment, because both parents and family physician were often hesitant to give vigorous treatment when the patient did not seem very ill. In addition, despite frequent presentation of the aims of the program, methods, and reasons for adequate treatment to the county medical society, some physicians treating the children of this group were apparently not well enough acquainted with the details of treatment. It must be admitted that some of the children, if not the majority, did not appear to have typical streptococcic sore throats when examined, and the physicians who saw them undoubtedly felt that they had a viral upper respiratory infection, with a coincidental positive throat culture. The commonest error in the group inadequately treated was to give an initial injection of procaine penicillin and a prescription for a sulfonamide to be taken later, or to follow up the initial injection of penicillin with inadequate oral penicillin.

Among other things, it was hoped that over a period of time enough cases would be found to answer the question as to whether rheumatic fever can be prevented in school children (on a public health basis) as well as in Air Force personnel. As there were no epidemics of streptococcic sore throat among the children studied, the number of positive cultures is obviously too small to draw any conclusions about rheumatic fever prevention. This same program, with some modifications, is being carried on with a different group of 12,000 school children during the present school year and will add to the total number of positive cultures. The large number of cultures taken and the time, energy, and money spent on the project would seem to make it impractical for a large-scale public health project. However, the same number of personnel involved in the program could handle a much larger number of children if cultures were taken on the "typical"

cases. We hesitated to do this, because we felt sure that a significant number of streptococcic sore throats would be missed, having been repeatedly impressed by those patients with acute rheumatic fever who on careful questioning give a history of only a mild sore throat or who have had no symptoms at all preceding the rheumatic fever. It may well be that concentrating on the sicker children could produce a satisfactory degree of rheumatic fever control in a community at a much lower cost and that, with some modifications, a similar plan could be incorporated into the public school health program.

There is no statistical answer as to whether the educational program stressing adequate penicillin therapy of streptococcic sore throat presented to teachers, parents, and physicians has helped in reducing the amount of rheumatic fever in this part of Ohio. However, we know that there are many children (and adults) in this area who would not have been treated previously but who now receive adequate penicillin therapy because of the increased awareness of physicians and parents brought about by the constant reminder of its importance through this program.

The prevention of rheumatic fever recurrences is a matter for cardiac clinics and individual supervision by a physician, but we are convinced that the prevention of first attacks of rheumatic fever is a least partly a community problem, because it involves every healthy child in the community. For this reason, during the school year of 1953-1954, in addition to the already established program in Mahoning County, the program was extended to adjacent counties. In Trumbull County, a Heart Association registered nurse, in close cooperation with the county medical society, school authorities, and board of health, set up a temporary program in any school where an epidemic of sore throat, scarlet fever, or other streptococcic disease arose. Here a similar educational program with school personnel, physicians, and parents was carried out, and, among other things, a simpler plan of detecting streptococcic sore throats in school children was attempted, with the use of the already existing school health facilities. Any child seen by the school nurse in the course of her usual duties who appeared to have a possible streptococcic sore throat was subjected to a throat culture, which was in turn taken to the Trumbull Memorial Hospital laboratory by the Heart Association nurse. In Columbiana County, where the public health nurse last year reported a high incidence of rheumatic fever, a plan of education in the preventive aspect of rheumatic fever was initiated in cooperation with the women's auxiliary of the county medical society.

SUMMARY

First attacks of rheumatic fever can be prevented by early adequate penicillin therapy of streptococcic sore throat in a large percentage of cases, and this can be done simply and cheaply if the person with the sore throat can be identified and if his physician is aware of the importance of correct treatment. One of the approaches to the problem is community education of parents, teachers, school nurses, and physicians, as has been done in three counties in northeastern Ohio.

Union National Bank Bldg. (3) (Dr. Bunn).

TREATMENT OF TYPHOID WITH SYNNEMATIN B

PRELIMINARY REPORT

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Synnematin was found by Gottshall and co-workers in 1951 [1] and separated into synnematin A and synnematin B by Olson and co-workers in 1953.[2] Mice were freed of Salmonella typhi and Salmonella typhimurium and chicks of Salmonella pullorum by treatment with synnematin B.[3] Olson and Holt demonstrated that synnematin B was not toxic for human beings,[4] and Olson found that synnematin B was effective against a wide variety of Salmonella strains in vitro.[5] Olarte and Figueredo tested five antibiotics against 40 strains of S. typhi in vitro and found synnematin B to be the most effective.[6] On the basis of these observations we decided to evaluate synnematin B in the treatment of typhoid in human patients. This is a preliminary report of the first clinical trial of this antibiotic in human beings.

SELECTION OF CASES AND CONTROLS

An attempt was made to select early, uncomplicated cases of typhoid for study, but this was not always possible. Diagnosis was established clinically and confirmed by laboratory methods before treatment. Sixteen children ranging from 2½ to 11 years of age were treated with synnematin B. The treated diseases consisted of 15 cases of typhoid and one case of paratyphoid A. Three cases were very severe, nine severe, and four moderate. Most of these patients were poorly nourished. The number of control patients was limited because of the general severity of the disease. There were six controls: three were

From the Hospital Infantil (Dr. Benavides), the Michigan Department of Health Laboratories (Drs. Olson and Holt), and the Instituto de Salubridad y Enfermadades Tropicales (Mr. Varela).

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2. Olson, B.; Jennings, J., and Junek, A.: Separation of Synnematin into Components A and B by Paper Chromatography, Science **117**:76, 1953.
3. Olson, B., and Jennings, J.: Effect of Synnematin B Treatment of Salmonella Infections in Mice and Chicks, Antibiotics & Chemother. **4**: 11, 1954.
4. Olson, B., and Holt, S.: Personal communication to the authors.
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untreated, one was treated with tetracycline, one was treated with tetracycline and chloramphenicol (Chloromycetin), and one was treated with synnematin B on the 26th day of the disease. Patients were kept in the hospital for observation for at least one month after the beginning of the disease. Thereafter, these patients returned to the hospital periodically for physical and laboratory examinations. The following laboratory determinations were performed on all patients during and after treatment:

Cultures of blood, feces, and urine
Agglutination tests
Complete blood cell counts
Chemical analyses of urine
Cephalin cholesterol, thymol, and Van den Bergh tests
Blood levels of urea, creatinine, sodium, and potassium
Sensitivity tests on all strains of S. typhi
Blood level of synnematin B during treatment
Urinary levels of synnematin B during treatment
Electrocardiograms

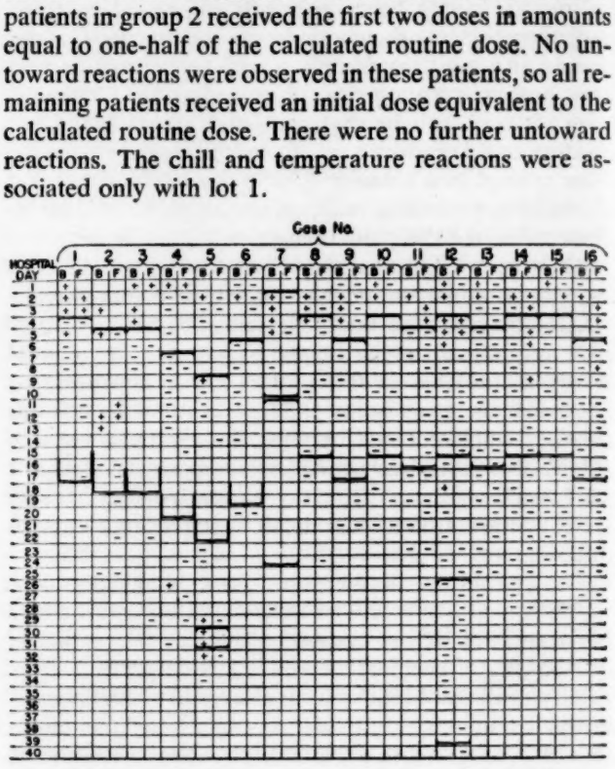
THERAPY

Dosage and Administration of Synnematin B.— The dosage of synnematin B was increased gradually as the study progressed, since there was no previous dosage experience in human beings with typhoid. Two lots of synnematin B were used, each containing about 25% of pure drug. Group 1 consisted of seven patients receiving 80 mg. per kilogram of body weight per day of lot 1 (20 mg. of pure synnematin B per kilogram per day). Group 2 consisted of four patients receiving 160 mg. per kilogram per day of lot 3 (40 mg. of pure synnematin B per kilogram per day). Group 3 consisted of five patients receiving 350 mg. per kilogram per day of lot 3 (87.5 mg. of pure synnematin B per kilogram per day).

TABLE 1.—*Clinical Responses of Sixteen Patients to Synnematin B Therapy*

	Dosage Schedule, Mg. per Kg. per Day		Response			
	Whole Drug	Synnematin B Content	Very Good	Good	Moderate	Poor
Group 1	80	20				
No. of patients			3	1	2	1
Case no.			1, 2, 3	6	4, 5	7
Group 2	160	40				
No. of patients			2	2	0	0
Case no.			8, 10	9, 11	..	..
Group 3	350	87.5				
No. of patients			3	1	0	1
Case no.			13, 15, 16	14	..	12
Total no. of patients			8	4	2	2

The original intention was to use a loading dose equivalent to one-third of the total dose for the first day. This schedule was used only in the patient in case 1 because the loading dose caused a severe chill and a marked elevation of temperature followed by a marked hypothermia. This reaction lasted for about one hour. The next four patients received no initial loading dose but still showed chills and temperature changes in lesser degrees. The next two patients received a starting dose of one-half of the calculated routine dose. The first three patients in group 2 received the first two doses in amounts equal to one-half of the calculated routine dose. No untoward reactions were observed in these patients, so all remaining patients received an initial dose equivalent to the calculated routine dose. There were no further untoward reactions. The chill and temperature reactions were associated only with lot 1.



Results of culture of blood and feces of patients with typhoid who were treated with synnematin B. The areas within braces represent the periods of treatment for each patient. "B" and "F" indicate determinations in blood and feces, respectively. In case 12 cultures of feces showed no organisms on the 44th and 46th days. The patient in case 13 had paratyphoid A.

All patients in group 1 received synnematin B for 14 days, with the exception of the patient in case 7 (9 days). Patients in groups 2 and 3 received synnematin B for 12 days. The patient in case 5 received a second course of synnematin B (2 days), while two patients (cases 7 and 12) received 14 day courses of chloramphenicol following synnematin B therapy. Synnematin B was reconstituted with sterile distilled water and administered every four hours intramuscularly in the buttocks.

Supportive Therapy.—All patients received adequate supportive treatment for dehydration, electrolyte imbalance, anemia, and myocarditis. All patients received a full diet throughout the course of illness without any additional commercial vitamins.[7] This diet consisted of varying quantities, depending on the patient's age, of milk, bread or tortillas, meats, fruits, cereals, and vegetables. Fluids (milk, fruit juices, and solutions) were forced by mouth or vein when necessary.

PROGRESS OF PATIENTS TREATED WITH SYNNEMATIN B

The response to synnematin B was similar in all patients but one (case 7). Regardless of the day of disease on which treatment began, the temperature returned to normal, the toxemia was relieved, the appetite increased, and the mental alertness improved in two to six days. In addition, there was a pronounced improvement in general well-being. We could not observe a definite pattern in the disappearance of fever. In some patients the fever

7. Gómez, F.; Ramos Galván, R.; Cravioto, J., and Frenk, S.: Studies on the Undernourished Child: 13. Treatment of Third Degree Malnutrition Without Commercial Vitamins, A. M. A. Am. J. Dis. Child. 87: 684 (June) 1954.

fell by crisis (cases 1, 8, and 15) and in others, by lysis (cases 2, 9, and 14) during the period of treatment. This was true despite the fact that three different dosage schedules were used. However, there was a distinct relationship between clinical response and dosage. With the exception of the patient in case 7, all patients were in good general condition at the completion of therapy. The classification of clinical responses is shown in table 1. There were no hemorrhages, perforations, or deaths. Data on the progress of the treated patients are shown in table 2.

Organisms in Blood and Feces.—The blood and feces culture findings before, during, and after treatment are shown in the figure. S. typhi disappeared from the blood and feces in every patient during treatment. With one exception (case 2) the blood and feces became free of the organism early in treatment, and in this case the blood and feces cleared before the end of treatment. In 13 of the 16 cases, the blood and feces remained organism free until the patient was discharged from the hospital. In three patients blood cultures were positive after the completion of therapy: in case 4 there was a single positive culture on the 6th day following treatment; in case 5 there were four consecutive positive cultures, on the 7th, 8th, 9th, and 10th days following treatment; and in case 12 there was a single positive culture after therapy with synnematin B was stopped. In none of the 16 were cultures of feces positive after treatment.

Agglutination Tests.—Agglutination tests were negative in case 5 during the patient's hospital stay. All other patients showed the expected agglutinin responses.[8]

Sensitivity of S. Typhi and S. Paratyphi A to Synnematin B.—All strains of S. typhi isolated from diagnostic cultures of blood were tested for sensitivity to synnematin B. Strains from 10 patients were sensitive to 1 unit of synnematin B; from 4 patients, to 0.5 unit; and from 1 patient, to 2 units (case 15). The strain of S. paratyphi A (case 13) was sensitive to 1 unit. The strains of S. typhi isolated after relapse of the disease showed no change in sensitivity from originally isolated strains.

Relapses.—Three of the 16 patients studied suffered relapses. Two relapses (cases 4 and 5) occurred in group 1, the exploratory dosage group, and one relapse (case 12) occurred in group 3.

CASE 4.—The patient was severely ill and fairly well nourished. Daily blood levels of synnematin B were around 1 unit per milliliter, which corresponded to the level of sensitivity of the organism recovered from the blood. Fever descended by lysis during treatment, and the clinical response was moderate. The temperature was normal for three days following therapy. At this time, a clinical and bacteriological relapse (one positive blood culture) occurred that lasted one week and subsided without additional therapy. The patient had an uneventful recovery.

CASE 5.—The patient was very severely ill and poorly nourished. Daily blood levels of synnematin B were around 0.5 unit per milliliter. The organism recovered from the blood at diagnosis was sensitive to 1 unit of synnematin B. Fever descended by lysis during treatment, and the clinical response was moderate. The temperature was normal for five days following therapy. A clinical and bacteriological relapse (four positive blood cultures) then occurred and lasted 10 days. An additional course of treatment with synnematin B was started but was discontinued in two days because of a marked leukopenia. The antibiotic was discontinued despite the facts that the fever was declining and the patient was showing clinical improvement. Penicillin was then given for eight days. The patient was discharged several days later in good condition and with improvement as shown by blood studies. This patient has not returned for a follow-up examination.

TABLE 2.—*Data on Treatment with Synnematin B of Fifteen Patients with Typhoid and Paratyphoid A*

Case No.	Sex	Age, Yr.	Day of Disease: Admission	First Positive Culture Before Treatment: Blood	First Positive Culture Before Treatment: Feces	Duration of Treatment	First Negative Culture After Beginning Treatment: Blood	First Negative Culture After Beginning Treatment: Feces	Last Day of Fever	Relapse	Discharge	Illness	Nutrition	Complications	Total Dose, Gm.	Dosage, Mg./Kg./Day
									Group 1							
1	F	11	5th	5th	6th	8-22	10th	15th	12th	....	34th	Severe	Fair	.....	22.7	76
2	M	8	15th	17th	....	19-33	30th	30th	32nd	....	49th	Severe	Fair	Myocarditis	22.4	80
3	F	10	10th	10th	10th	14-28	15th	15th	21st	....	40th	Moderate	Fair	Parotitis	16.8	50
4	M	11	8th	8th	8th	14-28	15th	15th	28th	33rd	53rd	Severe	Fair	.....	33.6	88
5	M	6	5th	6th	....	13-27 34-36	14th	18th	27th	33rd	49th	Very severe	Poor	.....	16.8	80
6	M	8	10th	11th	....	15-29	17th	29th	29th	....	32nd	Moderate	Poor	.....	13.4	90
7	M	5	8th	9th	....	9-18*	15th	12th	36th	....	39th	Very severe	Poor	.....	14.4	110
									Group 2							
8	F	9	22nd	23rd	....	25-37	31st	26th	31st	....	47th	Severe	Good	.....	56.8	175
9	F	11	7th	8th	....	12-24	13th	25th	23rd	....	29th	Moderate	Good	.....	56.8	160
10	M	6½	10th	10th	....	13-25	19th	19th	29th	....	34th	Severe	Poor	.....	31.2	176
11	M	2½	16th	17th	18th	20-32	22nd	21st	31st	....	42nd	Moderate	Poor	Glomerulonephritis	19.2	177
									Group 3							
12	F	8	24th	24th	27th	27-39†	31st	30th	64th	41st	71st	Very severe	Very poor	Myocarditis	57.6	370
13‡	M	5	8th	8th	....	12-24	13th	13th	21st	....	35th	Severe	Poor	.....	57.6	340
14	F	7	8th	9th	9th	11-22	13th	19th	31st	....	35th	Severe	Poor	Probable tuberculosis and myocarditis	57.6	340
15	M	2½	6th	6th	7th	9-21	10th	16th	23rd	....	39th	Severe	Poor	Myocarditis	46.0	384
16	M	5	6th	7th	8th	11-23	12th	14th	25th	....	36th	Severe	Poor	.....	57.6	370

* Chloramphenicol given from 18th to 32nd day of disease. A total of 7.1 gm. was given at the rate of 60 mg. per kilogram per day for the first seven days and 30 mg. per kilogram per day for the last seven days.
† Chloramphenicol given from 49th day to 63rd day of disease. A total of 11.9 gm. was given at the rate of 80 mg. per kilogram per day for the first seven days and 40 mg. per kilogram per day for the last seven days.
‡ Paratyphoid A.

8. Benavides V., L.; Carrillo, J., and Kumate, J.: Level Alterations of Circulating Antibodies with Antibiotic Treatment of Typhoid Fever, Bol. Med. Hosp. Infantil, to be published.

CASE 12.—The patient was very severely ill and very poorly nourished. Daily blood levels of synnematin B averaged 5.6 units per milliliter. The organisms recovered from the blood at diagnosis and during the relapse were sensitive to 1 unit of synnematin B. Fever descended by lysis during the first 10 days, and the clinical response was satisfactory. The temperature began to spike irregularly on the 12th day of treatment, and the patient's condition became worse. On the third day after the completion of therapy with synnematin B a positive culture of the blood was obtained, followed by three negative blood cultures. On the 10th day following treatment with synnematin B a clinical relapse occurred, and temperature rose to 104.5 F. Treatment was begun with chloramphenicol and continued for 14 days. Four days after the beginning of therapy with chloramphenicol, the temperature returned to normal and the patient's condition improved. The patient was discharged one week after the completion of therapy in good condition.

Poor Response to Antibiotics.—The patient in case 7 did not respond well to treatment with either synnematin B or chloramphenicol.

CASE 7.—The patient was very severely ill and poorly nourished. The organism recovered at diagnosis was sensitive to 1 unit of synnematin B and 2.5 mcg. of chloramphenicol. Although the fever showed a tendency to diminish, the clinical reaction of the patient was not considered satisfactory; on the ninth day of treatment with synnematin B, chloramphenicol was substituted. On the seventh day of the latter treatment the temperature became normal, but it rose again for the final seven days of treatment, when the dosage was reduced from 60 mg. to 30 mg. per kilogram per day. The temperature continued high for six more days and then became normal, and the patient was sent home in good condition. One month later the patient was found to be well, with a weight gain of 0.9 kg. and normal laboratory findings.

Paratyphoid A.—In case 13, the organism isolated from the patient's blood was S. paratyphi A and was sensitive to 1 unit of synnematin B. The blood level of synnematin B averaged 5 units per milliliter. Fever descended rapidly by crisis during treatment, and the clinical response was excellent.

Levels of Synnematin B in Blood and Urine.—Examples of blood levels of synnematin B are shown in table 3. Blood levels increased with increasing dosages of the drug, but not in direct proportion. The drug appeared to be rapidly excreted in the four hour period between injections. Examination of single specimens of urine from each patient showed very high concentrations of synnematin B. Patients 2 through 6 in group 1 had urinary levels of 6, 6, 6, 10, and 10 units per milliliter, respectively;

TABLE 3.—*Levels of Synnematin B in Blood of Treated Patients*

Day of Treatment	Time of Determination	Units per Ml.					
		Group 1		Group 2		Group 3	
		Case 3	Case 6	Case 9	Case 10	Case 12	Case 13*
1	2 hr. after 1st injection	0.9	0.18	0.50	0.5	3.7	2.9
	4 hr. after 1st injection	0.6	0.23	0.6	0.6	1.7	1.2
	2 hr. after 2nd injection	0.6	0.24	< 0.5	1.0	3.7	4.2
	4 hr. after 2nd injection	0.8	0.30	< 0.5	Not done	1.7	1.2
2	1 hr. after 1st injection	1.1	0.20	3.7	3.6	8.2	6.9
	2 hr. after 2nd injection	0.8	0.33	2.0	3.4	4.0	3.3
	3 hr. after 3rd injection	1.6	< 0.5	1.5	1.1	1.1	1.7
	4 hr. after 4th injection	1.4	< 0.5	Trace	1.4	1.7	1.1
3	1 hr. after 1st injection	2.2	< 0.5	2.5	3.5	5.5	7.4
4	1 hr. after 1st injection	1.6	0.6	5.2	2.2	6.4	5.4
5	1 hr. after 1st injection	2.2	0.5	3.0	3.1	4.7	4.8
6	1 hr. after 1st injection	1.0	< 0.5	5.8	4.6	6.0	4.7
7	1 hr. after 1st injection	0.6	0.5	4.2	2.4	6.0	5.6
8	1 hr. after 1st injection	1.3	0.9	4.1	3.6	8.0	4.2
9	1 hr. after 1st injection	0.6	0.7	4.5	4.2	4.5	5.2
10	1 hr. after 1st injection	0.9	0.4	2.1	0	7.3	4.7
11	1 hr. after 1st injection	1.4	0.5	5.0	4.0	4.2	3.3
12	1 hr. after 1st injection	1.0	0.5	5.5	4.0	4.2	5.0
13	1 hr. after each injection	1.2	0.5				
14	1 hr. after each injection	2.1	0.5				

* Paratyphoid A.

TABLE 4.—*Data on Six Control Patients with Typhoid*

Case No.	Sex	Age, Yr.	Day of Disease									No. of Negative Cultures Before Discharge	
			Admission	First Positive Culture Before Treatment		Duration of Treatment	Last Day of Fever	Discharge	Illness	Nutrition	Complications	Blood	Feces
				Blood	Feces								
17	F	11	30th	41st & 42nd	41st	.....	57th	68th	Severe	Good	.....	..	..
18	M	2	8th	8th, 9th, 10th, 14th	....	.....	45th	46th	Moderate	Poor	.....	10	12
19	M	4	26th	....	39th & 42nd	.....	53rd	59th	Severe	Poor	Myocarditis, intestinal hemorrhage	9	9
20	M	13	10th	11th	....	12-25, tetracycline	45th	49th	Severe	Good	.....	11	17
21	F	12	8th	8th	....	12-17, tetracycline; 17-31, chloramphenicol	28th	33rd	Severe	Fair	Myocarditis, intestinal hemorrhage	..	..
22	M	6	14th	15th	15th	26-34, synnematin B	40th	63rd	Very severe	Poor	Meibomianitis	10	13

patients in group 2 had levels of 400, 500, 700, and 512 units per milliliter; and patients in group 3 had levels of 35, 220, 270, 880, and 980 units per milliliter.

Toxicity.—We could not find any toxic reactions to the drug except the chill reaction observed generally at the beginning of treatment. This reaction was markedly reduced when lot 3 was used instead of lot 1.The reduction of the reaction was such that patients 11 through 16 received initial doses equal to the calculated routine dose. Local reactions observed consisted of pain at the site of injection in a number of patients and induration in one patient. Liver tests and chemical determinations in the blood showed normal liver and kidney function. Hemograms, electrocardiograms, chemical analysis of urine, and electrolyte determinations of blood were compatible with disease situations.

PROGRESS OF CONTROL PATIENTS

There were six control patients. Five of these were severely ill, while the sixth was moderately ill. The pertinent data on these patients appear in table 4. Three of these patients were not treated (cases 17, 18, and 19). Two patients were treated with tetracycline as soon as the diagnosis was established (cases 20 and 21). The patient in case 20 received tetracycline for 13 days (100 mg. per kilogram per day). The patient in case 21 received tetracycline for 5 days (50 mg. per kilogram per day) and then received chloramphenicol for 14 days (80 mg. per kilogram per day for the first 7 days and 40 mg. per kilogram per day for the last 7 days). It was our intention to include a fourth untreated patient, but his condition had so deteriorated on the 26th day of the disease that treatment was begun with synnematin B (case 22).

CASE 17.—The patient was admitted with profound fever, toxemia, and general malaise. Cultures of blood and feces were positive on the 41st day of disease. Fever persisted for 22 days (98.6 to 104 F) before the temperature returned to normal. Cultures of feces were sporadically positive during the course of the disease, with the last positive culture on the 59th day of the disease. The patient was discharged well after 38 days of hospitalization without antibiotic treatment.

CASE 18.—The patient was admitted with fever that persisted for 17 days, with an accompanying toxemia. There were four positive blood cultures on admission. During hospitalization all subsequent cultures of blood and feces were free of the organism. The patient was discharged after 38 days of hospitalization without antibiotic treatment.

CASE 19.—The patient was admitted with fever that persisted for 27 days. Diagnosis was established clinically and by positive agglutination test. The organism was present in the feces on the 39th and 42nd days of the disease. During the sixth week myocarditis and intestinal hemorrhage developed. Two cultures of blood and five of feces done after the 42nd day of disease were negative. Recovery was slow, and the patient was discharged after 33 days of hospitalization without antibiotic treatment.

CASE 20.—The patient was admitted with high temperature and toxemia. Culture of the blood on admission was positive. Therapy with tetracycline was begun immediately and continued for 13 days. The fever and toxemia persisted for three weeks despite therapy. Eight days after the discontinuance of therapy, the temperature dropped to 99.5 F and remained at this level for 15 days, spiking occasionally to 101.3 to 102.2 F. The patient was discharged after 39 days of hospitalization.

CASE 21.—The diagnosis was confirmed immediately with a positive culture of the patient's blood. Treatment was begun on the 12th day of disease with tetracycline but was stopped on the 5th day of therapy because of the critical condition of the patient. Therapy with chloramphenicol was begun and was continued for 14 days (80 mg. per kilogram for the first 7 days and 40 mg. per kilogram per day for the last 7 days). At the beginning of this course of treatment the patient had intestinal hemorrhage, vomiting, diarrhea, and myocarditis. The myocarditis persisted for nine days. The condition of the patient improved on the seventh day of treatment with chloramphenicol, and the patient was discharged well after 25 days of hospitalization.

CASE 22.—The patient was admitted with profound toxemia, dehydration, fever, and diarrhea. Cultures of blood and feces were positive on admission. Cultures of feces were also positive on the 20th and 23rd days of disease. The patient's condition gradually worsened despite supportive therapy, and there was intestinal hemorrhage. Treatment was begun with synnematin B on the 26th day of the disease on a dosage schedule of 400 mg. per kilogram per day, with the starting dose equal to the calculated routine dose. An intense, severe chill occurred with the initial dose, but 48 hours later the temperature was normal, toxemia had disappeared, and there was no further melena. Therapy was continued for eight days. The last finding of organisms in the feces was on the second day of treatment. Recovery was excellent, with the temperature remaining around 99.5 F until discharge after 49 days of hospitalization.

COMMENT

The management of typhoid is important in the Hospital Infantil because of the large number of patients with typhoid admitted annually. We have had wide experience with different types of treatment recommended for this disease. Chloramphenicol has been the drug of choice, although it has not proved to be ideal from every aspect of the disease. Woodward and others [9] have summarized the deficiencies of the drug as follows: "(1) Relapses occur in an appreciable proportion of treated cases; (2) S. typhosa may persist in the biliary tract and feces for variable periods of time; (3) the typhoid carrier state is not permanently cleared by chloramphenicol, and (4) the important complications of intestinal hemorrhage and perforation continue to occur." We therefore approached the clinical evaluation of synnematin B with interest. Of the 16 patients, 15 with typhoid and 1 with paratyphoid A, who were treated with varying dosages of the drug, the clinical response was very good in 8, good in 4, moderate in 2, and poor in 2 (table 1). We considered a very good response to be a marked clinical improvement with a rapid descent of temperature and clearance of organisms from feces and blood during and after treatment. A good response was one in which the clinical improvement and the clearance of blood and feces were satisfactory but fever showed a slower and more irregular decline. A moderate response consisted of a good clinical improvement and irregular decline of fever followed in a few days by a clinical and bacteriological relapse that subsided with no specific treatment. A poor response was indicated by slow clinical improvement and a slow or irregular decline of fever, with or without a relapse.

The two patients who had moderate clinical responses and one patient who had a poor response belonged to group 1, which we considered as the exploratory dosage group. The other patient with poor clinical response, who was in group 3, combined the severest clinical situation and the poorest nutritional condition encountered in the entire study. The clinical and laboratory results in groups 2 and 3 were closely comparable and far superior to those

9. Woodward, T.; Smadel, J., and Parker, R.: Symposium on Efficacy of New Drugs: The Therapy of Typhoid Fever, M. Clin. North America 38: 577, 1954.

in group 1. Thus, there was one unsatisfactory response in nine patients (total of groups 2 and 3) against three in the seven patients in group 1.

The figure shows the effect of synnematin B on presence of organisms in blood and feces in treated patients. Briefly, S. typhi disappeared from the blood and feces of every patient during treatment; S. typhi was recovered from the blood of 3 of the 16 patients after therapy; and S. typhi was never recovered from the feces of any patient after therapy. This is contrary to our experience and that of others with chloramphenicol.[10] On the basis of our observations in this short series of patients, it would appear that synnematin B is bactericidal rather than bacteriostatic. This aspect of synnematin B therapy will be further studied in the next series of patients.

We have attempted to follow the patients in this study after discharge from the hospital in order to determine the possibility of a carrier state. Thirteen patients have returned for examination over periods of from one week to three months (42 visits); all cultures of feces have shown absence of organisms, and agglutination tests have been in accord with the clinical picture of the disease. This indicates that none of these patients had become a carrier. We have been surprised to find that most of these patients were in excellent nutritional condition despite the fact that they were returned to their original environment. Many of them have shown the nutritional recovery syndrome described by Gómez and others.[11]

There were 3 relapses and 1 persistent case among the 16 cases studied. Two relapses and the persistent case were in patients in group 1. These results are not surprising, since the blood levels of synnematin B and sensitivity results in that group closely approximate each other. The third relapse occurred in a very poorly nourished, severely ill patient with daily average blood levels of 5.6 units per milliliter and an organism sensitivity of 1 unit per milliliter. We have observed that chronically malnourished children do not show the usual pattern of infection or of recovery. One patient who had a relapse recovered without additional treatment, the second recovered with a second course of synnematin B (two days) and penicillin (given because of a marked leukopenia), and the third recovered with a 14 day course of chloramphenicol following synnematin B therapy. The patient whose disease was resistant to treatment received a 9 day course of synnematin B followed immediately by a 14 day course of chloramphenicol and made a very slow recovery. We have no way of knowing the pattern of recovery had synnematin B been used instead of chloramphenicol in the second courses of treatment. Our data on blood levels and excretion of synnematin B indicate that the highest levels are attained in one hour after injection and that the drug is excreted rapidly by the fourth hour. Urinary concentrations were very high. Concentrations in blood and urine increased with increasing dosages.

There was no sign of toxic condition from the drug except the chill reaction. We are not sure whether the chill reaction and certain temperature elevations observed during the course of treatment were due to synnematin B or to impurities. It is significant that, in a number of patients, the temperature returned abruptly to normal as soon as treatment was stopped (cases 4, 5, 9, and 10). Conversely, two patients with hypothermic reactions had elevations of temperature after the initial injections of synnematin B (cases 6 and 11), and two other patients (cases 14 and 16) showed sudden, marked elevation of temperature immediately after injections of the drug during treatment, despite the good clinical response to the treatment. The possibility also exists that the chill reaction and temperature elevations were due to massive liberation of toxin.

In view of the good clinical response, the clearance of organisms from the blood and feces during therapy, the absence of any indication of the carrier state, and the lack of toxicity of the drug, it is our opinion that synnematin B, as observed in this short series of patients, should be considered an efficient therapeutic agent in the treatment and control of typhoid. We intend to continue our study with more highly purified synnematin B. Special attention will be given to dosage schedules, periods of treatment, and other routes of administration.

SUMMARY

A clinical trial of synnematin B in 15 patients with typhoid and 1 with paratyphoid A showed that this antibiotic has a specific effect in the disease. There were three relapses and one persistent case, in all of which recovery occurred. Two of the patients who had relapses were in the exploratory dose group. There were no intestinal hemorrhages, perforations, or deaths. The blood and feces of all patients were cleared of Salmonella typhi during the period of treatment. The carrier state was not observed in any patient up to three months after treatment. No toxic effects of the drug were observed except for a chill reaction with one lot of the drug.

10. Good, R., and Mackenzie, R.: Chloramphenicol in Typhoid Fever, Lancet **1**: 611, 1950. Cook, A., and Marmion, D.: Chloromycetin in the Treatment of Typhoid Fever, ibid. **2**: 975, 1949. Smadel, J.; Bailey, C., and Lewthwaite, R.: Synthetic and Fermentation Type Chloramphenicol (Chloromycetin) in Typhoid Fever: Prevention of Relapses by Adequate Treatment, Ann. Int. Med. **33**: 1, 1950.

11. Gómez, F.; Ramos Galván, R., and Cravioto, J.: Nutritional Recovery Syndrome: Preliminary Report, Pediatrics **10**: 513, 1952.

Koch's Postulates and Cancer.—Progress in overcoming the mystery concept of cancer is taking place at an increasingly rapid rate. Most important in this progress is the replacement of the melancholy and defeatist tradition by the constructive conviction that the cancer cell can be attacked as just another invading microorganism. It is now viewed by some as being as characteristically different from the normal body cell as is the pneumococcus or the tubercle bacillus, and so potentially as susceptible to selective chemical destruction. The most impressive evidence in support of this view is at hand in the modern procedures of growing human neoplastic cells outside of the human body because, by doing so, Koch's postulates can be fulfilled. Compliance with these requirements, laid down by Koch in 1880, has been and still is regarded as conclusive proof that a particular biologic entity is causative of a disease process, and that the destruction of the organism must be achieved if cure is to be attained. These postulates are three: (1) That the organism be demonstrable regularly in the diseased tissue itself; (2) That it be susceptible to culture outside of the body; (3) That it induce the characteristic disease when reinoculated. These postulates have now been fulfilled for the cancer cell in neoplastic disease as completely as they were for the tubercle bacillus in tuberculosis 70 years ago.—C. P. Rhoads, M.D., Pitfalls and Progress in Cancer Control, *Annals of Internal Medicine*, December, 1954.

DIAGNOSIS AND TREATMENT OF THE PAINFUL SHOULDER

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The diagnosis of lesions causing pain or limitation of motion in the shoulder is one of the difficult problems confronting the physiatrist. The symptoms and clinical signs are frequently so similar in many different pathological conditions that even the most careful study may fail to provide the correct diagnosis. Every painful shoulder will be the result either of a pathological change in the shoulder region itself or of a more distant lesion causing referred pain in the shoulder. Although this presentation is to emphasize restricted motion of the scapulohumeral joint, other joints of the shoulder girdle can also be implicated as causes of shoulder stiffness and pain.

Whenever the upper extremity is carried through a full range of motion at the shoulder level, movement occurs at the scapulohumeral joint, the acromioclavicular joint, and the sternoclavicular joint. The scapula itself moves in a rotatory fashion on the trunk. It articulates with the trunk only through the clavicle, which acts as a strut to maintain the radius of motion. Three groups of muscles act during shoulder motion: those passing from (1) the scapula to the humerus, (2) the trunk to the humerus, and (3) the trunk to the scapula. The long heads of the biceps and triceps cross the scapulohumeral joint but exert less effect on its motion because of the mechanical disadvantage under which they function. Of special interest is the small group of short rotator muscles that extend from the scapula to the humerus. They insert into the capsule of the joint and through it into the humerus, forming the floor of the bursa. Overlying the capsule and adjacent to the acromium, coracoid process, and muscular structures are several bursae. Although it was the most common diagnosis made in shoulder lesions 20 years ago, the diagnosis of bursitis is now infrequently made as a primary cause of shoulder disability. The cause of the disability usually exists in neighboring structures. The lesions more commonly associated with bursitis are rupture or avulsion of the supraspinatus or other short rotator tendons, calcification in the supraspinatus tendon, or irregular hypertrophic changes in the greater tuberosity of the humerus. Inman [1] has shown that the subscapularis. infraspinatus, and the teres minor act as depressors of the humerus during abduction and flexion of the arm. The supraspinatus and deltoideus act simultaneuosly during abduction. During the first 30 degrees of abduction the scapula attains a position of stability. Beyond 30 degrees of abduction, for every 15 degrees of motion, 10 degrees occurs at the scapulohumeral joint and 5 degrees by rotation of the scapula on the thorax. Motion at the acromioclavicular joint occurs at the beginning of abduction and after 135 degrees of abduction. From a clinical standpoint measurements of the shoulder motion are taken in forward flexion, abduction, extension, and rotation. Measurement of the scapulohumeral motion is made in abduction. One arm of the goniometer is placed on the arm and the other in the axillary line, which is parallel to the vertebral border of the scapula. With the examiner's fingers on the lower angle of the scapula, the humerus is gently abducted until the scapula begins to move laterally. The angle between the humerus and the scapula is then measured to determine the amount of scapulohumeral motion. Normal shoulder motion is not possible if this angle measures less than 90 degrees. If scapulohumeral motion is limited the patient invariably elevates the shoulder when attempting to abduct the arm, thus defeating the purpose of active shoulder exercise.

DIFFERENTIAL DIAGNOSIS

The causes of shoulder pain are numerous. They have been listed by Coventry [2] according to systems involved, namely, musculoskeletal, neurological, visceral, and peripheral vascular. From a practical point of view in relation to the treatment required, the more common causes may be classified according to the presence or absence of limitation of motion. Group 1, pain without limitation of motion, may result from: (1) cervical hypertrophic arthritis, (2) protrusion of cervical disk, (3) tumor of the cervical cord, (4) abnormal posture, (5) metastatic tumors of the neck, (6) whiplash injury of the cervical spine, (7) cervical rib, (8) scalenus syndrome, and (9) visceral referred pain. It is obvious that patients with shoulder pains, the causes of which are classified in group 1, will not respond to treatment directed toward the shoulder. Treatment should be directed toward the removal or relief of the causative factor. If the patient has a history of radiation of pain, especially paresthesias in the forearm and fingers, and if roentgenographic evidence of degenerative changes of the cervical spine with or without impingement on the foramina is present, we have found that the most effective management is heat, usually diathermy, followed by massage for relaxation and then by suspension using the Sayre head sling and very strong traction in the erect position. Occasionally a protruded cervical intervertebral disk will have to be removed. Postural abnormalities that have been included in the term scapulocostal syndrome show restricted motion of the scapulothoracic articulation. Limitation of motion may occur secondarily at the scapulohumeral joint.

Group 2, limitation of shoulder motion, is usually found in the following conditions: 1. Calcified tendinitis. During the acute phase of the disorder the symptoms respond to x-ray therapy or hydrocortisone acetate injections locally. In the chronic phase hot packs, massage, and assisted active motion have been beneficial. 2. Periarthritis (frozen shoulder). 3. Bicipital syndrome. The tendon sheath of the long head of the biceps descends 2.5

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1. Inman, V. T.; Saunders, J. B. deC. M., and Abbott, L. C.: Observations on the Function of the Shoulder Joint, J. Bone & Joint Surg. 26: 1-30 (Jan.) 1944.

2. Coventry, M. B.: Problem of Painful Shoulder, J. A. M. A. 151: 177-185 (Jan. 17) 1953.

in. below the joint proper. The tendon may be involved in any inflammation of the shoulder by virtue of its proximity. There may also be anomalies of the biceps groove. This syndrome has recently become more commonly recognized. Some authors have contended that degeneration of the tendon of the biceps is the primary cause for the prolongation of disability from the frozen shoulder and have advised surgical transplantation of the long head of the biceps to the point of origin of the short head when conservative measures fail. Hydrocortisone acetate injected into the point of maximal tenderness and followed by physical therapy has often been successful. 4. Reflex sympathetic dystrophy. The shoulder-hand syndrome has been treated successfully with the usual physical treatment plus sympathetic blocks and/or cortisone. 5. Partial degeneration of the short rotator cuff. This usually responds to avoidance of the precipitating movements plus physical therapy. 6. Immobilizing lesions of the upper extremity such as Colles' fracture, hemiplegia, or radical mastectomy. These frequently cause restricted motion at the scapulohumeral joint. 7. Arthritis of the shoulder joint and of the acromioclavicular joint. Specific measures such as salicylates, cortisone, or x-ray therapy must be used concurrently with physical therapy if there is persistent major restriction of motion. 8. Paralytic conditions, such as axillary nerve injury. These are treated to maintain range of motion. Electrical stimulation to maintain muscle volume is necessary. 9. The severely involved shoulder in patients with poliomyelitis. If untreated, this will invariably present restriction of scapulohumeral joint motion. Hot packs and stretching are imperative in the treatment program.

When acute pain decreases, some patients gradually achieve full range of motion without specific physical procedures. More often, especially when motion is markedly decreased, intensive physical therapy is necessary. After treatment with hot packs and by massage, the scapulohumeral joint is gradually mobilized with assistive active motion and mild passive stretching. The scapula must be stabilized by the therapist during motions of the arm. Mild traction and rotation of the arm is also applied with the scapula stabilized. It is absolutely essential that this type of treatment be given by a therapist or, at least, by someone other than the patient. The usual prescription of active exercise to be done by the patient at home is ineffective, because the limitation of scapulohumeral motion causes the shoulder to be elevated in active exercise. Thus, the motion performed is actually humerothoracic with the scapulohumeral joint unchanged in range of motion. The therapist must hold the scapula firmly in position while the scapulohumeral motion is carried out passively or actively in order to gain range of motion in that joint. Devices for stabilization of the scapula have not been successful in our experience. Motion of the scapulohumeral joint to 80 degrees or more and total range of thoracohumeral motion to 110 degrees or more should be obtained before the patient is allowed an entirely self-conducted exercise program. Active resistive exercises in all planes, stressing rotatory movements, should be carried out before therapy is discontinued.

SUMMARY

The symptoms and clinical signs of the various causal factors of restricted scapulohumeral joint motion are often so similar that it is difficult to provide the correct diagnosis. The more common causes of shoulder pain are classified according to pain with and without restriction of scapulohumeral joint motion. Mobilization of the scapulohumeral joint by manual stabilization of the scapula during active or passive exercise is necessary. Optimal return of shoulder function has been observed in those patients who received intensive treatment until at least 80 degrees of scapulohumeral motion and 110 degrees of thoracohumeral motion was obtained before starting a home exercise program.

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PRESENT VALUE OF ULTRASONIC DIATHERMY

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Under therapeutic conditions most biological reactions to ultrasound are due essentially to the heating produced by absorption of ultrasonic energy.[1] Nonthermal effects also have been observed.[2] Their therapeutic significance is, as yet, poorly understood. Other reactions, such as cavitation, have been found to be destructive phenomena.[3] They occur only at higher intensities than those used with proper techniques in therapy. Therefore, it seems justifiable to consider ultrasonic therapy primarily as a form of diathermy. However, ultrasonic diathermy has some distinctive features. A specific distribution of temperature in the tissues is caused by a selective absorption of the energy in some tissues.[4] As a result, certain anatomic structures such as bones, joints, nerves, and tendons are heated selectively. Furthermore, owing to the short wave length of ultrasound it is comparatively easy to direct and limit the treatment to a certain area. Although ultrasound is a very efficient method of heating the deep tissues, it has a shortcoming. The rise of temperature occurs so quickly that precautions have to be taken to avoid overheating. Since it is debatable whether the selective rise of temperature in the depth of the tissues is more beneficial than other forms of heating, the final value of ultrasound as a therapeutic agent can

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The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

1. Lehmann, J. F.: The Biophysical Mode of Action of Biologic and Therapeutic Ultrasonic Reactions, J. Acoustical Soc. Am. 25: 17-25 (Jan.) 1953.

only be determined by clinical studies. Many clinical investigations have been performed.[5] Most of the authors were favorably impressed by the results of these studies. Unfortunately, only very few investigators critically compared the results with those obtained in controls. Therefore, final evaluation of the therapeutic efficacy of ultrasound is, as yet, impossible.

STATISTICAL STUDY

Since statistical analyses comparing the effects of ultrasound with those obtained with other accepted forms of diathermy are required for an assessment of the value of ultrasonic diathermy, we have attempted such a study. Seventy-eight patients who had periarthritis of the shoulder were treated with ultrasonic energy. The results obtained in this group were compared with those in another group of 72 patients who had received treatment with microwave diathermy. Both groups of patients received sedative massage and identical exercise programs after the application of heat. Applications of ultrasound were made once a day for 5 to 10 minutes. The ultrasonic frequencies used were 1 or 0.8 megacycle per second. The radiating surfaces of the applicators were 5 to 7 sq. cm. A continuous total output of 2.5 to 14 watts was applied with a stroking technique in such a fashion that the temperature of the periarticular tissues was just below that which will cause periosteal pain. The microwaves were applied to the shoulders with the "B director" (6 in. hemispheric type) for 30 minutes once or twice a day.

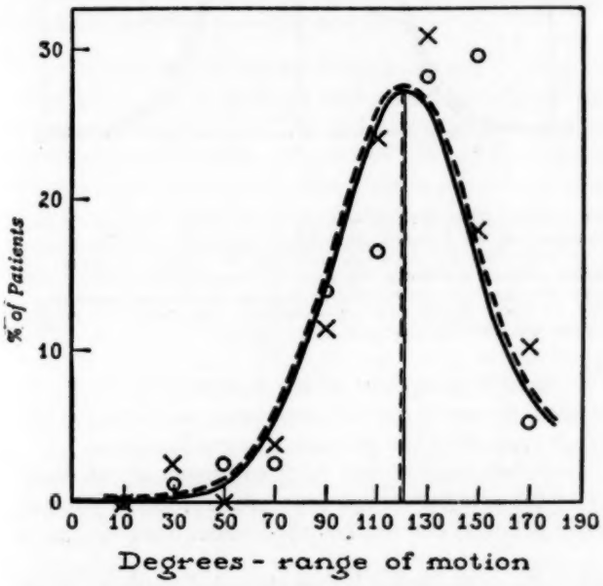

Fig. 1.—Calculated distribution of the range of forward flexion before treatment in the groups of patients with periarthritis of the shoulder later treated with ultrasound (solid line) and microwaves (dotted line). Data observed in the ultrasound-treated group are indicated by circles; its mean and standard deviation are 129.9 ± 29.0 degrees. Data observed in the microwave-treated group are indicated by crosses; its mean and standard deviation are 121.1 ± 29.3 degrees. (Reproduced with permission of the *Archives of Physical Medicine and Rehabilitation*).

The selected output of the machine was 40 to 100% of the maximal output. The patients in each group were treated for the same number of days (average, eight days). In order to rule out psychological effects, all patients in each group were told that they received "a new type of diathermy treatment."

The statistical evaluation was based on the measurements of the range of motion before the first and after the last treatment. For this statistical comparison it was necessary for us to deal with a random distribution of

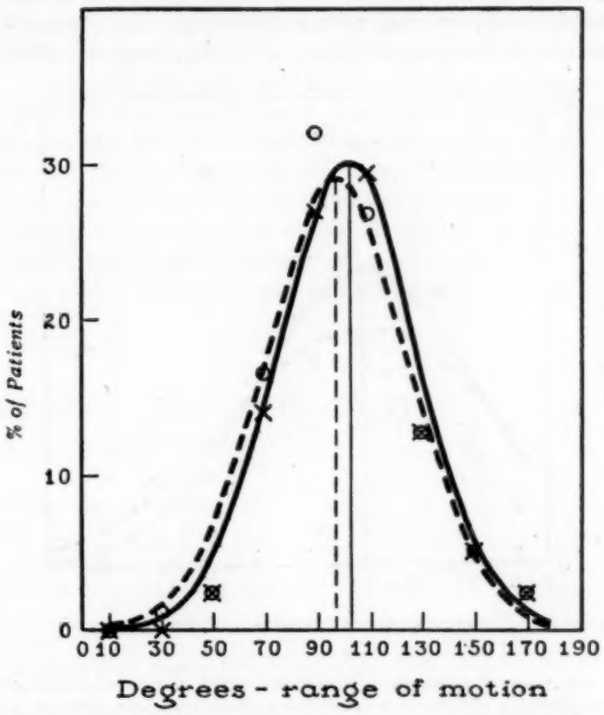

Fig. 2.—Calculated distribution of the range of abduction before treatment in the groups of patients with periarthritis of the shoulder later treated with ultrasound (solid line) and microwaves (dotted line). Data observed in the ultrasound-treated group are indicated by circles; its mean and standard deviation are 103.4 ± 26.5 degrees. Data observed in the microwave-treated group are indicated by crosses; its mean and standard deviation are 96.8 ± 27.8 degrees. (Reproduced with permission of the *Archives of Physical Medicine and Rehabilitation*.)

the measured ranges of motion. This requirement was fulfilled, since the calculated distribution curves satisfactorily fitted the observed data, within the limits of the statistical error. Furthermore, it was imperative to make

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5. Lehmann, J. F.: Present Status of Ultrasonic Therapy, Arch. Phys. Med. **34**: 741-748 (Dec.) 1953. Lehmann, J. F.; Erickson, D. J.; Martin, G. M., and Krusen, F. H.: Comparison of Ultrasonic and Microwave Diathermy in the Physical Treatment of Periarthritis of the Shoulder (Study of the Effects of Ultrasonic and Microwave Diathermy When Employed in Conjunction with Massage and Exercise), ibid. **35**: 627-634 (Oct.) 1954. Aldes, J. H.; Jadeson, W. J., and Grabinski, S.: A New Approach to the Treatment of Subdeltoid Bursitis, Am. J. Phys. Med. **33**: 79-88 (Feb.) 1954. Mueller, E. E.; Mead, S.; Schulz, B. F., and Vaden, M. R.: A Placebo-Controlled Study of Ultrasound Treatment for Periarthritis, ibid. **33**: 31-35 (Feb.) 1954. Krusen, F. H.: Present Status of the Use of Ultrasonic Energy in Physical Medicine, South. M. J. **45**: 55-60 (Jan.) 1952. Present Status of Use of Ultrasonic Energy in Physical Medicine, report of the Council on Physical Medicine and Rehabilitation, J. A. M. A. **148**: 646-651 (Feb. 23) 1952. Statistik über mit Ultraschall erzielte Heilerfolge, Ultraschall in der Medizin **1**: 389, 1949. Friedland, F.; Bisgrove, J. G., and Doyle, B. J.: Therapeutic Application of Ultrasonic Energy, Arch. Phys. Med. **33**: 461-466 (Aug.) 1952. Bierman, W.: Ultrasound in Treatment of Scars, ibid. **35**: 209-214 (April) 1954.

sure that the type and the extent of the disorder in one group were as similar as possible to those in the other. Therefore, distribution curves of the various ranges of motion before treatment (fig. 1, 2, and 3), of the duration of the symptoms prior to the patient's admission to the hospital (fig. 4), and of the age groups (fig. 5) were calculated from the observed data. The corresponding curves in each group of patients were compared. The degree of overlapping of the curves was considered as an indication of their similarity. Within the limits of the statistical error, the distribution curves of the group of patients selected for treatment with ultrasound were identical with the corresponding curves obtained in the group of patients selected for treatment with microwaves. The ratio of male to female patients was 1:1.5 in the group receiving ultrasonic treatment and 1:1.8 in the group treated with microwaves. In addition, all patients in each group complained of various degrees of pain; about 15% of each group had stated that they had received roentgen therapy prior to admission; and about 45% of each group had had physical therapy elsewhere.

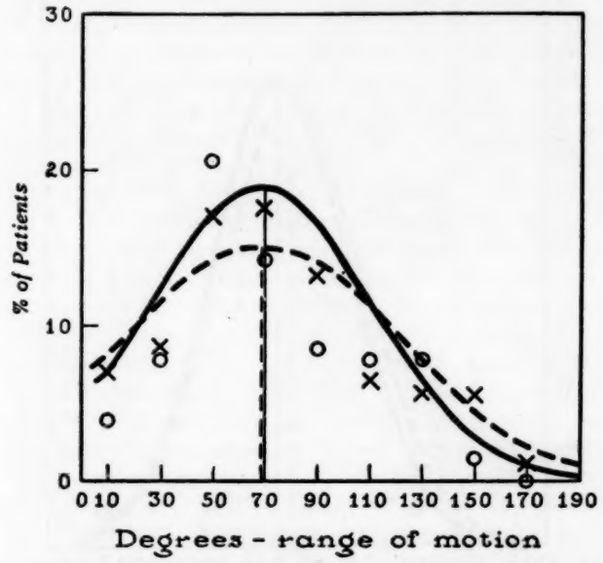

Fig. 3.—Calculated distribution of the range of rotation before treatment in the groups of patients with periarthritis of the shoulder later treated with ultrasound (solid line) and microwaves (dotted line). Data observed in the ultrasound-treated group are indicated by circles; its mean and standard deviation are 68.7 ± 42.3 degrees. Data observed in the microwave-treated group are indicated by crosses; its mean and standard deviation are 68.6 ± 38.8 degrees. (Reproduced with permission of the *Archives of Physical Medicine and Rehabilitation.*)

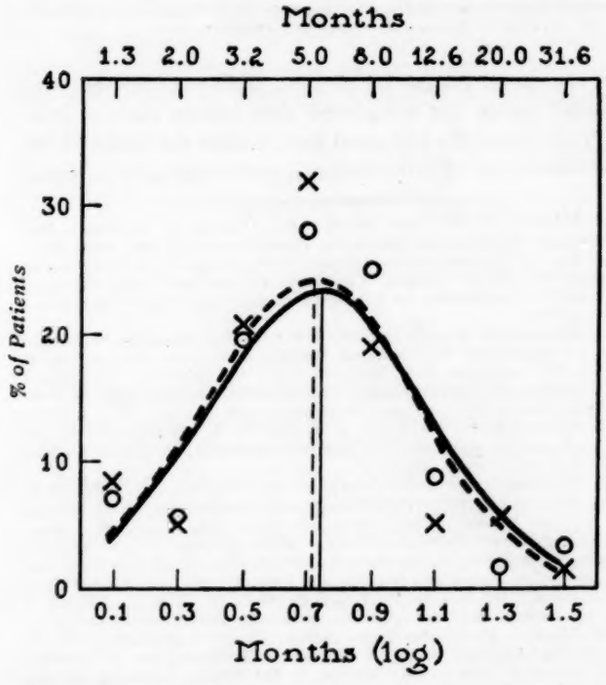

Fig. 4.—Calculated distribution of the duration of symptoms prior to the admission to the clinic in the groups of patients later treated with ultrasound (solid line) and microwaves (dotted line). Data observed in the ultrasound-treated group are indicated by circles; its mean and standard deviation are log (5.4 months) ± log (2.19 months). Data observed in the microwave-treated group are indicated by crosses; its mean and standard deviation are log (5.2 months) ± log (2.22 months). (Reproduced with permission of the *Archives of Physical Medicine and Rehabilitation.*)

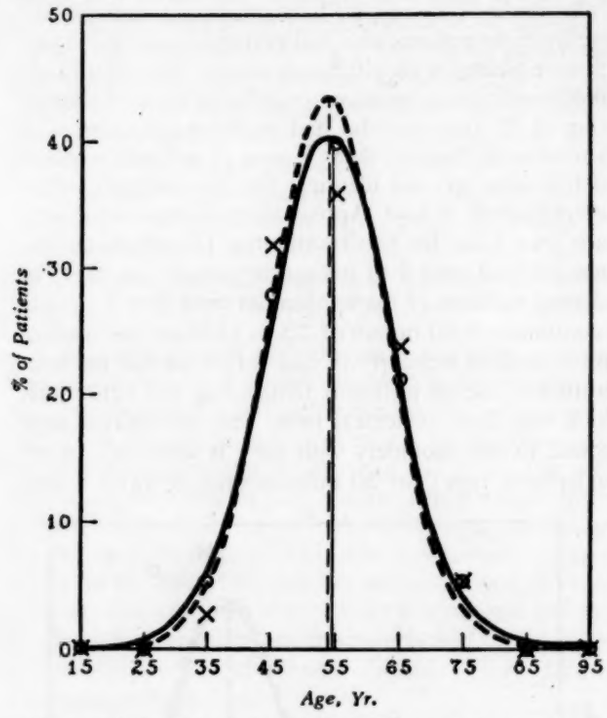

Fig. 5.—Calculated distribution of age in the groups of patients treated with ultrasound (solid line) and microwaves (dotted line). Data observed in the ultrasound-treated group are indicated by circles; its mean and standard deviation are 54.2 ± 9.9 years. Data observed in the microwave-treated group are indicated by crosses; its mean and standard deviation are 53.9 ± 9.1 years. (Reproduced with permission of the *Archives of Physical Medicine and Rehabilitation.*)

These data suggest that, prior to treatment, the duration of the symptoms, age distribution, ratio of male to female patients, and degrees of shoulder involvement in each group were similar enough to permit a statistical comparison between the results obtained by ultrasonic therapy plus massage and exercise in one group and the results of microwave diathermy plus massage and exercise in the other group. The results shown in the table

Gain in Range of Motion in Patients with Periarthritis of the Shoulder After Ultrasonic and Microwave Treatment

Motion	Gain in Degrees After Treatment with: Ultrasound	Microwaves
Forward flexion	27.4 ± 2.3*	16.1 ± 1.5
Abduction	32.6 ± 2.5	21.2 ± 2.1
Rotation	45.4 ± 2.8	17.3 ± 4.0

* Standard error of the mean.

indicate that the gain in the range of motion was somewhat greater when ultrasound was used than when microwaves were used. The difference is statistically significant. Almost all patients in each group had variable improvement of the subjective complaints.

COMMENT

These results may be interpreted as suggesting that ultrasonic diathermy plus massage and exercise is more efficient in the treatment of periarthritis of the shoulder than microwave diathermy plus massage and exercise, at least with regard to the gain in range of motion. However, this statistical evaluation does not give any information on how much more efficient ultrasound is; therefore, it still is debatable whether ultrasonic therapy should be given preference to the other forms of diathermy. Clinical observation and the tabulated data suggest, at least, that ultrasound can be used effectively by a physician skilled in its application. The role of ultrasound in the treatment of periarthritis of the shoulder can be considered similar to that of any other form of heat treatment: ultrasonic therapy plus massage and exercise often relieves pain and mobilizes the joint.

Ultrasonic therapy seems to be a valuable therapeutic adjunct if it is properly used as a form of diathermy in conjunction with an adequate program of other types of physical therapy. However, much more research must be done in order to refute or corroborate the claims published in the literature. A careful determination of indications and contraindications must be made before the value of this new therapeutic agent can finally be assessed.

LONG-TERM MANAGEMENT OF HYPERTENSION WITH PENTOLINIUM TARTRATE (ANSOLYSEN)

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and
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The recent release of pentolinium tartrate (Ansolysen) to the medical profession prompts us to add our experience with this new and valuable agent to that already published [1] in the hope that maximal clinical advantage can be taken of this powerful new drug.

SERIES OF THIRTY-ONE PATIENTS

Selection.—Only patients with one or more of the serious complications of hypertensive disease or with diastolic blood pressures consistently above 120 mm. Hg on repeated determinations were selected for long-term treatment. Ten of these 31 patients had previously had sympathectomy, since it is our belief that supradiaphragmatic sympathectomy still has a place in the treatment of rapidly progressive, severe hypertensive disease.[2] No patients in whom therapy was instituted have been excluded from this study. Thus, the results to be described include our successes and failures indiscriminately.

Determination of Dosage.—Since this was an attempt at long-continued management, we sought the maximal control of the blood pressure compatible with the demands of ordinary daily living. Therefore, we administered the drug orally, except for a few patients who, for reasons of uremia or the necessity of nocturnal control of the blood pressure, took one or more doses by injection. In some patients who appeared to absorb the drug very poorly, one-twentieth of the oral dose was effective when given parenterally. Dosage was regulated in most cases by the blood pressure response observed at the clinic during all-day visits, rather than by data obtained from the patient after instructing him in taking his own blood pressures. Usually, initial dosage adjustment was established in the hospital and further adjustment made during four to six clinic visits, at gradually increasing intervals, until the response became stabilized. To prevent constipation, variable absorption, and possible subsequent ileus, we directed the patient to take a laxative daily, usually magnesia magma or cascara rather than bulk-forming laxatives, and to omit the pentolinium if constipation lasted more than 24 hours. To protect against increased sensitivity to ganglionic blockade, which may occur after large meals, alcohol, heavy work, excessive heat, or colds and other infections, we followed Professor Smirk's advice and instructed the patient to omit or reduce any oral or parenteral dose of pentolinium if, just prior to the time of administration, motionless standing for one minute induced marked dizziness. To determine the magnitude of blood pressure reduction, we observed the patient in the clinic for three to seven hours, taking blood pressures with the patient lying and standing every half hour. The patient remained seated and ambulatory between readings. The lowest blood pressure determination usually occurred in the afternoon, and we made every effort to bring the standing blood pressure at this time to the lowest level compatible with the patient's well-being. The dose that proved effective in the clinic did not seem excessive at home as judged by the reported frequency of dizziness on standing. We therefore feel that blood pressure values taken in the office under these conditions are reasonably representative of

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From the University Hospital, Department of Internal Medicine, University of Michigan Medical School (Dr. Hoobler). Research Fellow of the Michigan Heart Association (Dr. Agrest).

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The pentolinium tartrate (Ansolysen) used in this study was furnished through Dr. D. L. Shaw, Wyeth Laboratories, Philadelphia.

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Results of Therapy with Pentolinium Tartrate in a Consecutive Series of Patients with Severe Hypertension

Case No.	Sex	Age, Yr.	Therapy: Duration, Mo.	Therapy: Final Daily Dose, Mg.	Therapy: Other Treatment	Therapy: Side-Effects, Severity *	Average Blood Pressures Before and After Taking Pentolinium, Mm. Hg †: Standing: Before	Standing: After	Recumbent: Before	Recumbent: After	Complications	Remarks
1	F	46	9	600	Reserpine	1	172/110§	160/96	172/110	176/98	Coronary thrombosis	Systolic blood pressure 250 mm. Hg on first visit
2	F	43	9	540	Reserpine, splanchnicectomy	2	247/144§	192/124	247/144	200/130	.....	Late tolerance
3	M	48	9	600	Reserpine	1	235/130§	182/96	235/130	201/101	Coronary thrombosis, transient focal cerebrovascular episodes	.....
4	F	42	9	600	.....	1	190/120	120/78	195/120	142/88	.....	.....
5	F	49	7	300	Splanchnicectomy	3	226/134§	117/77	226/134	181/109	Congestive heart failure	No congestive heart failure
6	M	42	7	300	.....	4	233/152	197/124	246/148	223/144	Transient focal cerebrovascular episodes, uremia	Died of cerebrovascular lesion; poor control
7	M	39	7	174‡	Hydralazine	2	190/102	198/108	199/119	208/110	Congestive heart failure	Congestive heart failure improved; marked tolerance
8	F	41	7	22.5‡	Reserpine	1	194/107§	148/95	194/107	177/103	.....	Blood pressure 230/248-114/129 mm. Hg on first visit
9	M	46	7	450	Reserpine, splanchnicectomy	2	226/118	178/88	243/113	217/113	Congestive heart failure	Dyspnea relieved
10	M	45	7	360	Reserpine, splanchnicectomy	2	202/130	138/90	219/137	174/108	.....	.....
11	M	52	7	300	.....	4	180/130	183/125	230/134	191/123	.....	Discontinued therapy because of postural dizziness
12	F	33	6	360	Reserpine, splanchnicectomy	0	211/121§	162/114	211/121	216/122	.....	.....
13	F	35	6	180	Splanchnicectomy	1	180/130	120/100	184/120	179/104	.....	.....
14	F	58	6	120	Reserpine	1	226/111§	142/78	226/111	176/84	Retinopathy interfering with gross vision	Retinopathy improved; blood pressure on admission 300 mm. Hg
15	F	45	5	300	.....	0	245/110§	151/98	245/110	174/98	Transient focal cerebrovascular episodes	.....
16	M	57	5	150	Reserpine	2	208/107§	158/89	208/107	176/90	Coronary thrombosis	Occasional angina; blood pressure decline owing to reserpine
17	M	52	5	75‡	Hydralazine	0	280/138§	192/100	280/138	206/100	Congestive heart failure, uremia	Nonprotein nitrogen level fell; no congestive heart failure
18	M	45	5	300	Splanchnicectomy	0	220/143	167/118	224/133	215/124	Transient focal cerebrovascular episodes	.....
19	M	35	4	67.5‡	Hydralazine	1	251/149§	110/73	251/149	174/111	Congestive heart failure, uremia, retinopathy interfering with gross vision	Nonprotein nitrogen level fell; patient improved; no congestive heart failure
20	M	42	4	540	.....	1	210/142§	176/124	210/142	194/130	Transient focal cerebrovascular episodes	.....
21	M	50	4	600	.....	1	191/121	120/82	232/120	158/99	.....	.....
22	F	50	3	240	Reserpine	2	200/118§	134/96	200/118	167/101	Transient focal cerebrovascular episodes	.....
23	M	49	3	240	Splanchnicectomy	1	240/144	169/108	232/134	186/112	Retinopathy interfering with gross vision	No recurrence of retinal thrombosis
24	M	54	3	180	Reserpine	1	258/124	182/112	247/120	202/118	Congestive heart failure	Congestive heart failure relieved
25	M	48	3	540	Reserpine	0	220/121	161/108	225/127	183/115	Transient focal cerebrovascular episodes	.....
26	F	46	3	150	Splanchnicectomy	4	235/132§	105/95	235/132	147/97	Coronary thrombosis	Congestive heart failure improved
27	M	37	2	240	Reserpine, splanchnicectomy	0	157/107	107/79	194/112	154/90	Congestive heart failure	Congestive heart failure relieved
28	M	37	2	300	Reserpine	3	194/128	154/102	202/118	190/110	Congestive heart failure	Congestive heart failure cleared completely
29	M	52	3	300	.....	3	254/144	124/74	272/156	210/106	Retinopathy interfering with gross vision; uremia	Long-standing uremia; died
30	M	33	1	12‡	Reserpine	0	194/158	195/132	244/136	200/133	Uremia	Uremic course unaffected; died
31	F	35	1	45‡	.....	1	204/124	200/128	223/118	218/114	Congestive heart failure	Also mitral and aortic insufficiency; pentolinium nightly relieved dyspnea

* Severity of side-effects is graded as follows: Constipation, dizziness, or fatigue for which the dose of pentolinium had to be reduced 2 to 3 times per week is grade 4 severity; 1 to 2 times per week, grade 3; and zero to 1 time per week, grade 2 or grade 1.

† Average of all readings taken half-hourly during a clinic visit. "Before" refers to the last determination before therapy was started; "after" refers to the latest visit during therapy. ‡ Subcutaneously.

§ No determination was made of blood pressure with the patient standing before therapy was started. The value found before therapy with the patient recumbent has been substituted for purposes of comparison.

the blood pressure of the patient at home. There is little doubt that ganglionic blocking agents do not abolish the pressor effects of stressful experiences. However, we believe that a fair approximation of the lowest daily home blood pressure value could be obtained by placing the patient in a quiet room on his arrival at the physician's office and obtaining readings with the patient in the lying and standing positions after a period of about 30 minutes of "rest." The time at which this observation should be made is most critical, since one should attempt to adjust the lowest daily blood pressure to the lowest levels compatible with the patient's well-being. We have found that the combined effects of a dose of pentolinium taken in the morning plus the noon meal produce a blood pressure "trough" at about 2 to 3 p. m., if the drug is taken right before breakfast and luncheon is eaten at 1 p. m.

Therapy.—Treatment was started by the administration of 20 mg. of pentolinium tartrate at 8 a. m., 3 p. m., and 10 p. m. daily; the dose was increased each day by 20 mg. increments until a lowest systolic blood pressure of 110 to 130 mm. Hg with the patient standing was achieved consistently and without disturbance of the normal daily bowel movements. After some experience was gained in the management of the individual patients, it was possible to lower this minimal systolic blood pressure to 90 to 100 mm. Hg if the medicament was well tolerated by the patient and, thus, to secure an even greater measure of control of the average blood pressure throughout the day. Episodes of constipation markedly enhanced the effect of the drug and, particularly at the beginning of therapy, resulted in very irregular control. Strict attention to bowel function in the early phases of treatment was most important, and we insisted on daily administration of magnesia magma or cascara, particularly at the initiation of treatment. At outpatient visits a 20 mg. increment in the dose of pentolinium was recommended if "trough" blood pressures had fallen almost to the desired level. If results were far short of satisfactory, the patient was instructed to increase his dose by an additional 20 mg. at three day intervals until the next visit, using the test of motionless standing to control possible overdosage.

Reserpine (Serpasil), 0.25 mg. three times daily, was given as additional medication in most cases. If the level of blood pressure determined in the morning with the patient recumbent fell under therapy, the reduction was attributed to the reserpine. If, after two or three months' trial, no reduction in this value occurred despite evident bradycardia and symptomatic side-effects of reserpine, the use of this agent was abandoned. Hydralazine (Apresoline) in doses up to 75 to 150 mg. four times daily was occasionally given in conjunction with pentolinium, but we rarely saw useful additive effects from this form of combined therapy, and, it was abandoned in all but three cases (cases 7, 17, and 19). No attempt will be made in this paper to distinguish the effects of addition or withdrawal of these medicaments to the regimen. The program will be evaluated in its entirety.

OBSERVATIONS

Analysis of our experience with pentolinium tartrate is presented from three standpoints: (1) improvement in complications, (2) side-effects of treatment, and (3) blood-pressure-lowering effects. A summary of the outcome of treatment in the 31 patients studied is presented in the table.

Complications.—Congestive heart failure was controlled in all of the nine patients who had presented this complication initially. Four patients who had had episodes of coronary thrombosis in the past tolerated therapy without complications. Precordial distress or pain resembling angina in severely hypertensive and nervous women was improved when the blood pressure was lowered, although typical exertional angina accompanying moderate hypertension in men was little affected by this form of treatment. Of the seven patients who had had cerebrovascular episodes, six remained free of further attacks for a total of 29 patient-months (4.8 months per patient). One cerebral hemorrhage occurred during therapy in a patient whose response to treatment was not particularly satisfactory (case 6). Five patients with uremia (nonprotein nitrogen between 48 and 81 mg. per 100 cc.) were treated, and three of them have died. The remaining two appear to have become stabilized, and their nonprotein nitrogen levels have remained the same or fallen. We have not made systematic observations on retinopathy; of four patients in whom it was a disabling presenting symptom, three have improved.

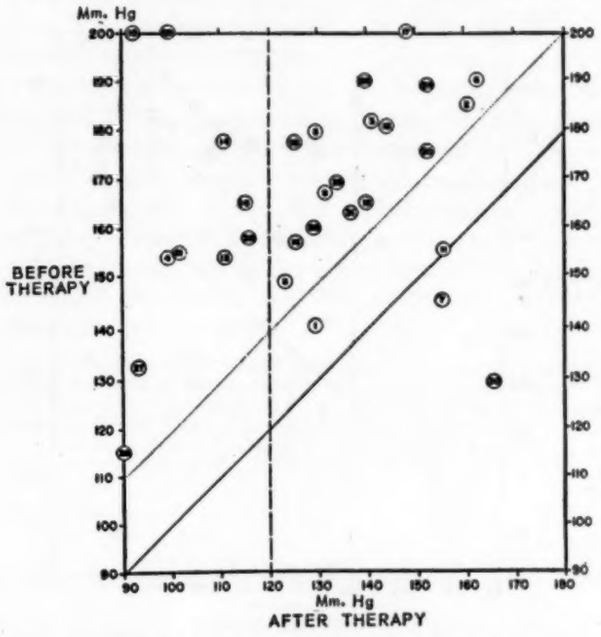

Fig. 1.—Effect of therapy with pentolinium tartrate and reserpine on mean standing blood pressure of hypertensive patients. Mean standing blood pressure is defined as one-half the sum of systolic and diastolic readings taken with the patient standing at half-hourly intervals during periods of three to seven hours spent in the clinic before institution of treatment and at the latest visit during treatment. Points falling on the solid diagonal line represent no change in mean all-day standing blood pressure as a result of treatment; points above the dotted line indicate decrease in pressure of more than 20 mm. Hg; and points to the left of the interrupted line indicate reduction of blood pressure to normal.

Side-Effects.—While none of our patients has been entirely free of side-effects of the medicament, most feel they are not a serious limitation and have returned to limited activity or to their old occupations. With increasing familiarity with the drug, they have become accustomed to occasional episodes of blurred vision, constipation, and orthostatic hypotension. In only one case were

the variability in response and the frequency of orthostatic hypotension sufficient to justify discontinuing treatment. Impotence was observed by all the male patients. The extent of weakness and lassitude varied considerably from one patient to another, but in general it was worse in those with the more serious complications of the disease. Occasionally, reduction or omission of the dose of reserpine relieved this complaint.

Reduction of Blood Pressure.—Figures 1 and 2 show the effects of therapy on the mean blood pressure. These data are chosen to represent the mean reduction in pressure load if the patient were to remain in the standing position or the recumbent position throughout the day. It must be recognized that the usual blood pressure actually occurring in the patient, which more closely approximates the level found with the patient in the seated position, is about halfway between the pressures indicated by the recumbent and standing readings, so the reduction in

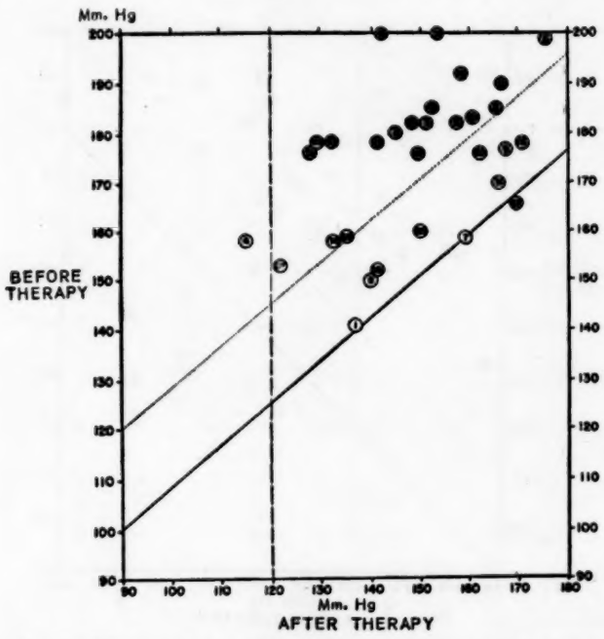

Fig. 2.—Effect of therapy with pentolinium tartrate and reserpine on mean recumbent blood pressure of hypertensive patients. Mean recumbent blood pressure is defined as one-half the sum of systolic and diastolic readings taken with the patient recumbent at half-hourly intervals during periods of three to seven hours spent in the clinic before institution of treatment and at the latest visit during treatment. Points falling on the solid diagonal line represent no change in mean all-day recumbent blood pressure as a result of treatment; points above the dotted line indicate decrease in pressure of more than 20 mm. Hg; and points to the left of the interrupted line indicate reduction of blood pressure to normal.

the daytime pressure load is probably less than that shown in figure 1 and more than that shown in figure 2. The reduction in mean recumbent blood pressure (fig. 2) probably represents the degree of reduction in nighttime blood pressure achieved by treatment. Normalization of the mean standing blood pressure is shown to have been achieved in 31% of the patients and reduction of pressure of more than 20 mm. Hg, in 87%. The median reduction was 38 mm. Hg. On the other hand, the blood pressure with the patient recumbent became normal after treatment in only one of the patients, but even for this posture in 68% of the patients it fell more than 20 mm. Hg. The median reduction in recumbent blood pressure was 23 mm. Hg.

COMMENT

Our experience indicates that a significant and continuing reduction in blood pressure can be produced by meticulous management of the hypertensive patient with orally administered pentolinium tartrate and reserpine. There have been no serious complications in patients given this therapy, and in only one case did unpleasant side-effects make it necessary to discontinue treatment. Tolerance is slow to develop and does not present the problem it does with hexamethonium salts, probably because of the larger amounts of the latter agent that must be given orally and that produce locally irritating effects on the gastrointestinal tract.

Success of Management of Hypertension.—The effect on the patient's actual daily blood pressure, of course, cannot be measured, but, if 68% of the patients have rereductions of pressure of 20 mm. Hg or more in a recumbent position and 56% have average daily blood pressure reductions of more than 40 mm. Hg in the standing position, it is probable that a significant effect has been achieved. If one assumes that the average blood pressure during the day is halfway between values found with the patient standing and sitting, then this value was reduced in our patients by 30 mm. Hg (median reduction of recorded mean pressure). The tabulation of the data required the lowest pretreatment blood pressures determined to be used; these were usually found after the patient had had several days of bed rest at the hospital and were often many millimeters below the blood pressures recorded under conditions of stress. While after treatment stressful experience still raised the blood pressure, it may be presumed that, since such rises start from a lower level, they are less likely to reach dangerous heights.

Recumbent blood pressure was less significantly affected. This treatment cannot, therefore, be said to provide adequate protection at night. This is probably the greatest defect in the regimen, and we are seeking methods to circumvent it. Elevating the head of the bed, as recommended by Professor Smirk, has had little effect in our experience unless the elevation is such as to produce almost a seated position at night. Following the lines suggested to us by Professor McMichael, we have recently attempted, in selected cases, to give a subcutaneous injection at night sufficient to lower the blood pressure with the patient recumbent to normal levels, with the hope that by morning the orthostatic effects would not be so extreme as to prevent ambulation. This has been successful in a few cases. We have also used protoveratrines A and B orally at bedtime, since this drug continues to be effective in the methonium-tolerant patient and lowers the blood pressure equally with the patient in the recumbent or the standing position.[2] An effect on the blood pressure of a patient when recumbent is achieved only when a marked effect on his blood pressure when standing is secured, and in most cases the discrepancy is so great that, to secure a significant reduction in recumbent blood pressure, a standing level below limits tolerable to the patient must be obtained. This discrepancy varies greatly among patients; it appears that splanchnicectomy increases the differential, thus allowing control of standing blood pressure with smaller doses but causing the drug to affect recumbent levels less significantly.

Other Cardiovascular Effects.—The effects on the complications of hypertensive disease are clearer. We have the definite impression that the drug has been lifesaving in four patients (cases 7, 9, 17, and 19) who had overwhelming cardiac failure. It has probably postponed incipient failure in others. The period of observation of patients with prior cerebrovascular episodes is not yet long enough to measure the effect of such treatment on the recurrence of cerebrovascular complications; however, the recent demonstration that in rats the reduction of pressure may in itself prevent or relieve focal cerebrovascular spasm [3] provides a theoretical basis for expecting that continued control of the blood pressure would delay or prevent this serious complication. The cause of such focal cerebral attacks is not clear. Perhaps too often they have been ascribed to simple thrombosis and attempts to lower the blood pressure viewed as dangerous. Although at first we were reluctant to attempt treatment of persons with a history suggestive of cerebrovascular "thrombosis," we now hesitate less if the pressure is very high, a trial of treatment is well tolerated, the patient is not obviously arteriosclerotic, and there is no major residual neurological lesion. We reason that the alternative of no hypotensive treatment is almost certain to lead to further, and probably fatal, cerebral attacks.[4]

That significant reductions in daytime blood pressure can be achieved by this therapy can hardly be doubted. It is probable that when marked lowering of the recumbent blood pressure is also accomplished the prognosis will be accordingly improved, as is suggested by Corcoran and others.[5] In order to achieve maximal reductions in recumbent pressure, we have found that it is necessary to force the lowest or "trough" blood pressure in the daytime to the lowest possible level compatible with the patient's well-being. It should be emphasized that, to achieve this therapeutic goal, meticulous and continuous observation is necessary. Treatment must be carefully individualized, and it is necessary to adjust the dosage continually until the greatest possible reductions in blood pressure are achieved. While this may seem tedious and difficult to the patient and doctor alike, it is possible for the intelligent practitioner following the principles summarized in this paper to obtain very great advantages from this form of therapy for hypertensive disease. It will never be satisfactory to place a patient on an ineffective dosage and hope for any benefit whatsoever to accrue in the long-term management of this disease.

SUMMARY

Thirty-one consecutive patients with severe or complicated hypertensive disease were treated with orally administered pentolinium tartrate (Ansolysen), with or without reserpine (Serpasil) and hydralazine (Apresoline). This was found to be a simple and safe regimen for the ambulatory management of hypertensive patients. A median reduction of 38 mm. Hg in the mean daytime standing blood pressure and of 23 mm. Hg in the mean recumbent blood pressure was estimated to have occurred. Notable improvement in the manifestations of congestive heart failure and of hypertensive retinopathy was observed. The effect of treatment on cerebrovascular complications was less certain but seemed beneficial. No marked relief of moderate uremia or of angina pectoris was seen.

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4. Pearson, E., and Hoobler, S. W.: Observations on the Prognosis After Hypertensive Cerebrovascular Episodes, unpublished data.
5. Corcoran, A. C.; Dustan, H. P.; Taylor, R. D., and Page, I. H.: Management of Hypertensive Disease, Am. J. Med. **17**: 383, 1954.

PHOTOFLUOROGRAPHY AT A U. S. NAVAL SHIPYARD

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Mass roentgenographic techniques for detecting chest diseases have become increasingly popular in the past decade. Surveys of large populations have been made possible by rapid and inexpensive methods of processing roentgenograms. The present survey, for the year 1953, was conducted at the New York Naval Shipyard, where chest roentgenograms have been taken annually of all civilian employees since 1949. Until 1951, 35 mm. films were taken; the use of 70 mm. photofluorograms was substituted at that time. The primary purpose of the chest survey at this establishment is the detection and control of tuberculosis. The problem is twofold: (1) the detection of tuberculosis in applicants for employment and (2) the detection of tuberculosis among employees.

Because of their small size, 35 mm. and 70 mm. photofluorograms have been suspected of missing minimal lesions. This misunderstanding has been clarified by a study [1] of 1,256 persons, in each of whom 35 mm., 4 by 10 in., 14 by 17 in. paper, and 14 by 17 in. celluloid chest films were taken within a few minutes of one another. These films were subsequently reviewed by five examiners independently. No one method was superior for case-finding purposes. Although the full-size films are necessary for diagnostic purposes, they hold no advantage over the smaller films for screening purposes. In all methods the percentage of interpretation error is high. Of 1,807 photofluorograms read 10 times,[2] a single reader missed an average of 32.2% of the lesions. The single reader, thus, detected only 68% of the disease present. If the films were reviewed by the same or another reader, a total of 84% of the lesions was discovered. Whatever size of film is used in mass chest roentgenography, it is apparent that all films should be re-

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The opinions set forth in this article are those of Dr. Guild and do not represent an official view of the Medical Department of the U. S. Navy or of the Navy at large.

1. Birkelo, C. C., and others: Tuberculosis Case Finding: Comparison of Effectiveness of Various Roentgenographic and Photofluorographic Methods, J. A. M. A. **133**: 359-366 (Feb. 8) 1947.
2. Roentgen Chest Surveys in Campaign Against Tuberculosis, editorial, J. A. M. A. **149**: 841-842 (June 28) 1952.

viewed after the initial reading. There is, moreover, a wide difference of opinion among trained readers as to normal and abnormal films, both 70 mm. and 14 by 17 in. In the series noted previously,[1] in 1,256 14 by 17 in. celluloid films interpreted one reader discovered 56 abnormal films and another, 100. Overreading, the suspicion of an inflammatory lesion on a 70 mm. photofluorogram that on a 14 by 17 in. film proves to be inactive or normal, is the major disadvantage to the use of small films. Overreading is the reason why from 1.7% [2] to 65% [3] of 14 by 17 in. films are requested.

The survey films have been effective in detecting pulmonary, cardiac, bony, and even high abdominal lesions. Of 400,263 35 mm. films taken of Navy men at the Great Lakes Training Station,[3] 8.49% showed abnormality. The age range of this apparently healthy group was 17 to 45 years, most being aged 18 to 35. These abnormal findings were: pulmonary, 7%; cardiac, 0.6%; and bony, 0.7%. In a more random population of 10,549 films,[4] 486 or 4.5% showed abnormalities of the cardiac silhouette (enlarged heart, abnormal configuration, or distorted aortic shadow). Of these patients 80% had organic heart disease as defined by the American Heart Association.

METHOD

The data below represent a series of 20,379 photofluorograms taken of civilian production workers and office personnel during 1953 at the New York Naval Shipyard. These films are divided into three groups:

Annual survey	18,146
Preemployment	2,161
Separation or retirement	72
Total	20,379

Not included in this series is a group of patients periodically followed with 14 by 17 in. roentgenograms because of lesions discovered on earlier annual surveys. These patients do not have annual photofluorograms taken. Only patients with previously normal photofluorograms are followed on the annual survey. Only the preemployment group had not had films taken here before.

The age distribution of the population of this shipyard is as follows.

Under 30	15.7%
31 to 40	31.3%
41 to 50	24.3%
51 and older	28.7%

The 70 mm. photofluorograms are read initially at the Naval Shipyard medical department and subsequently reviewed at the Bureau of Medicine and Surgery in Washington, D. C. In all doubtful cases, namely, cases in which the true nature of the process cannot be clearly defined on the 70 mm. film, a 14 by 17 in. celluloid film is taken. These 14 by 17 in. films are retained at the Navy Yard for comparison with future films and are not reviewed at the Bureau of Medicine and Surgery. If the 70 mm. photofluorograms clearly show abnormal but insignificant conditions such as calcifications or congenital rib defects, such defects are noted, but 14 by 17 in. films are not taken.

3. Mason, M. W.: Photofluorography for Chest Surveys, Radiology 43: 499-503 (Nov.) 1944.

4. Schwartz, B., and Berman, B.: Incidence of Heart Disease in Mass X-Ray Surveys, J. A. M. A. 149: 734-735 (June 21) 1952.

RESULTS

Abnormalities were found in 9.9% of all photofluorograms, the remaining 90.1% being interpreted as normal. Three per cent, or 602 photofluorograms, were sufficiently "suspicious" to warrant repeat filming of the subjects on 14 by 17 in. celluloid films. The results of the 602 requested reexposures on 14 by 17 in. films were distributed as follows.

Nondisqualifying defects	316
Required further clinical study	134
Normal	115
No repeat film taken because of transfer, separation, or like cause	37
Total	602

Nondisqualifying defects are those lesions diagnosed on 14 by 17 in. films that required no further clinical study. Several films contained more than a single lesion. The tabulation of nondisqualifying defects follows.

Apical caps or apical thickening	79
Increased bronchovascular markings	48
Hilar calcifications	20
Primary complex	18
Tuberculosis, minimal, inactive	18
Tortuous aorta	17
Ghon tubercle	16
Healed peripheral calcifications	15
Old fibrotic scars	15
Blunted costophrenic angles	14
Scoliosis	9
Pulmonary emphysema	7
Pulmonary fibrosis	6
Prominent minor fissure	6
Calcified aortic knob	6
Scalloping of the diaphragm	4
Surgical defects of the ribs	4
Miscellaneous	30

Miscellaneous findings were foreign bodies, calcified hematomas, azygous lobes, synarthroses, synostoses, old rib fractures, cervical ribs, thoracoplasty, dextrocardia, thoracic vertebral arthritis, and pericardial fat pads.

In 134 cases further clinical study was required either to establish more clearly a diagnosis or to elucidate more fully the seriousness of the problem. This clinical follow-up was performed by local hospitals, by chest clinics of local boards of health, and, when a history and physical examination sufficed, by the shipyard dispensary. In a few cases the private physician did the complete study. The principal diagnoses in this group were:

Tuberculosis, pulmonary, arrested	32
Fibrotic parenchymal or pleural scars of unknown cause	15
Pneumonia	8
Hypertensive cardiovascular disease	7
Pulmonary fibrosis of unknown cause	7
Rheumatic heart disease	6
Pulmonary emphysema	5
Tuberculosis, pulmonary, active	5
Bronchiectasis	3
Congenital heart disease	2
Scoliosis	2
Sarcoidosis	2
Ununited fracture of the clavicle	2
Apical caps	2
Increased bronchovascular markings	2
Carcinoma of the breast, metastatic	2
No evidence of disease	2

There was also one case of each of the following lesions: fibrous dysplasia of the rib, Ghon tubercle, healed peripheral calcifications, pneumoconiosis, large pericardial fat pad, cleidocranial dysostosis, substernal thyroid, spontaneous pneumothorax, bronchogenic carcinoma, diaphragmatic hernia, and bronchial cyst. There was no

follow-up in 19 cases. Of the five cases of active pulmonary tuberculosis, three were detected in the annual and two in the preemployment survey.

Yard workers with previously "suspicious" photofluorograms do not have films made on the annual photofluorographic survey but are followed solely with 14 by 17 in. films. The population under study was screened one year ago and found to have normal chests. Therefore, all lesions of a serious nature, such as carcinoma and active tuberculosis, were presumably not detectable one year ago.

SUMMARY

During the 1953 annual chest survey at the New York Naval Shipyard, 20,379 70 mm. photofluorograms were taken. Follow-up of the 602 "suspicious" photofluorograms in this series was done by taking 14 by 17 in. roentgenograms of the chest. Active tuberculosis was proved in five cases; two on preemployment films, and three on the annual survey of employees.

721 Huntington Ave. (15).

CLINICAL NOTES

ARTHRITIS FOLLOWING USE OF DESOXYCORTICOSTERONE ACETATE AND CORTISONE

OCCURRENCE IN PATIENT WITH ADRENAL CORTICAL HYPOFUNCTION

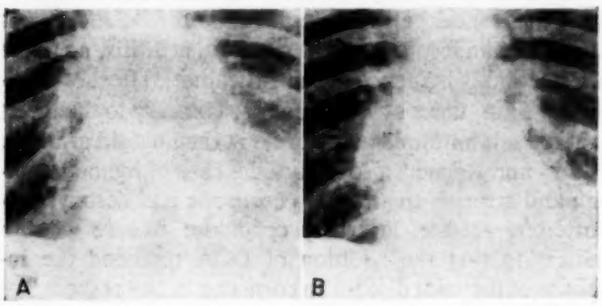
Lieut. Col. Laurence M. Hursh (MC), U. S. Army

Adrenal cortical hypofunction (Addison's disease) and arthritis rarely occur together in a patient.[1] The case presented in this paper is particularly rare, since the arthritis was aggravated by treatment with desoxycorticosterone acetate. Selye knows of only six similar cases,[2] and I have found only the one reported in this study.

REPORT OF A CASE

A 47-year-old woman was first seen on Feb. 19, 1952. She complained of being weak and resembled a textbook picture of adrenal cortical hypofunction. The patient was in good health until Nov. 10, 1951, when a radical mastectomy of the right breast was performed for a grade 3 carcinoma. Her postoperative course included anorexia, nausea, and vomiting; however, glucose, administered intravenously, improved her condition. In January, 1952, nausea, vomiting, and anorexia recurred, along with a marked intolerance to cold. The patient noted some darkening of her complexion in November, 1951, but since that time her skin had become much more pigmented over the exposed parts of her body. There had been no increased desire for salt. She was given cascara sagrada after surgery, as she had been constipated. She had had emotional lability and dizziness since mastectomy in November, 1951. Since Feb. 9, 1952, her chief complaint had been severe fatigue; she had been completely unable to walk up one flight of stairs. She had lost 30 lb. (13.6 kg.) since December, 1951. Her history included tuberculous peritonitis, diagnosed through laparotomy in 1930. The patient's right ovary and a cystic mass in the left breast were removed in 1937, and in 1940 radium therapy was given for metrorrhagia. The patient had had amenorrhea since July, 1951, and her blood pressure just prior to surgery in November, 1951, was 130/90 mm. Hg. Physical examination on admission revealed a pale woman, 5 ft. 9 in. (175 cm.) tall, weighing 120 lb. (54.4 kg.) (ideal weight, 159 lb. [72.1 kg.]), who was completely exhausted and able to speak only short phrases with great exertion. Her blood pressure was 85/50 mm. Hg. Her pulse rate was 110 beats per minute and difficult to obtain because of the compressibility of the radial arteries. The right breast was absent, and pigmentation was marked at the usual sites. The fasting blood sugar level was 69 mg. per 100 cc.

Clinical Course.—The patient was put to bed in a warm room, and, although she was covered with three blankets, she complained bitterly of being cold. Roentgenograms of the chest are shown in the figure, *A*. An electrocardiogram showed left axis of minus 30 degrees, a QRS complex of 0.12 second and ST segment depression and T-wave inversion in V_1, V_2, V_3, V_4, V_5, and V_6. She vomited all intake. It was then realized she had



Roentgenograms of the chest. *A*, prior to therapy. *B*, after therapy with desoxycorticosterone acetate and cortisone.

acute adrenal cortical hypofunction, so a polythene tube was inserted in a vein of the right arm, and a continuous drip of 5% glucose isotonic sodium chloride solution was started at 10 a. m. on Feb. 20, 1952. Daily doses of 125 mg. of cortisone were administered intramuscularly at this time. She showed a very dramatic response, and by Feb. 22 the nausea and vomiting had gone. The patient retained small amounts of food and was cheerful. A roentgenogram of the abdomen failed to reveal any calcification of the adrenals.

Desoxycorticosterone acetate was not available until Feb. 25, when 1 mg. daily was given. The patient's condition improved continuously and by Feb. 28 her blood pressure was 100/60 mm. Hg. At this time there was a slight suggestion of a moon-shaped face and the first signs of edema, with the patient weighing 132.25 lb. (60 kg.). By March 4 the electrocardiogram again showed left axis of minus 30 degrees and a QRS complex of 0.08 second. The T waves in V_3, V_4, V_5, and V_6 had now become upright, while those in V_1 and V_2 were flat. There was still slight sagging of the ST segments in V_5 and V_6. The roentgenogram of the chest at this stage is shown in the figure, *B*.

On April 1, 1952, 200 mg. of desoxycorticosterone acetate was injected below the right scapula. On April 10, 1952, 38 days after cortisone therapy was discontinued, emesis, fatigue, arthritic pains in the hips and thighs, and depression developed. Oral doses of the injectable type of cortisone were reinstituted (25 mg. daily) on April 11, 1952. This produced an immediate response, particularly with regard to the arthritis. The patient's fasting blood sugar level was now 92.5 mg. per 100 cc. On May 1 attempts were made to reduce the doses of cortisone from 25 mg. to 12.5 mg. daily. However, with this reduction the patient had recurring pains of arthritis, which, although not as severe as those previously complained of, were present for the next several months. By November, 1952, it was necessary to increase the doses of cortisone to control the patient's fatigue.

COMMENT

Selye postulates that the rheumatic diseases could be due to an excessive production of electrolyte hormones during stress, on the basis that treatment with desoxycor-

From the Student Detachment, Walter Reed Army Medical Center, Washington, D. C.

1. Caughney, J. E., and McCoy, J. E.: Addison's Disease with Associated Polyarthritis: Aetiological Study of Arthritis Syndrome, Brit. M. J. 2: 1189 (Nov. 17) 1951.

2. Selye, H.: The Story of the Adaptation Syndrome, Montreal, Canada, Acta, Inc., Medical Publishers, 1952, p. 193.

ticosterone acetate has produced rheumatic-like joint lesions in patients with adrenal cortical hypofunction. He further states that, although this does occur, it does not prove that desoxycorticosterone acetate usually causes this disease, nor even that it participates in the pathogenesis of the disease; but it does show that desoxycorticosterone acetate can be the cause of such joint lesions in man.[2] Thorn [3] has stated that in patients with adrenal cortical hypofunction treatment with desoxycorticosterone acetate does not produce arthritis with any regularity, and when such patients develop joint pains these are not clearly correlated with the hormone intake. Bauer [4] also stated that desoxycorticosterone acetate does not aggravate the joint lesions of patients with rheumatoid arthritis. Haydu,[5] however, reports: "We noticed repeatedly that DCA administered alone to rheumatoid arthritis patients brought about an aggravation of their condition." Bauer and Clark [4] state that "the administration of DCA does not alter the manifestations of rheumatoid arthritis, nor does it unfavorably influence the anti-rheumatic effect of cortisone." Thus, these observations are contrary to the thesis that the salt hormone plays a role in rheumatoid arthritis. Perera and Ragan [6] also reported a case of hypoadrenalism and arthritis treated with cortisone and desoxycorticosterone acetate, and they conclude: "There was no indication that the addition of DCA modified the response of the joint disease to cortisone in any respect."

Ellman and Cudkowicz [7] reported on a patient with adrenal cortical hypofunction and rheumatoid arthritis treated with desoxycorticosterone acetate and cortisone, and they made what appear to me to be contradictory statements. After treatment was started with desoxycorticosterone acetate, they state: "Rapid exacerbation of wrist swelling and tenderness and painful enlargement of the epitrochlear glands took place in the early part of the course." They further state: "DCA had no effect on the joint manifestations." Others, however, have not had these same experiences. For example, Caughney and McCoy [1] in 1951 were able to show that subsequent treatment with cortisone made joint lesions caused by desoxycorticosterone acetate disappear. It has been stressed that the clinical association of adrenal cortical hypofunction and rheumatic joint lesions is notably infrequent, in spite of the free administration of desoxycorticosterone acetate and salt to many patients with adrenal cortical hypofunction. Caughney and McCoy also quote others (Dejean, 1947; de Gennes and associates, 1947; and Laroche, 1947) who have reported the presence of adrenal cortical hypofunction with rheumatic joint lesions in patients treated with desoxycorticosterone acetate. Caughney and McCoy believe, however, that, provided there is a preexisting tendency in a person to develop rheumatic joint lesions, a significant aggravating factor in the pathogenesis of these lesions is an imbalance between the mineralocortocoids and the glucocorticoids.

SUMMARY

In the case reported, the patient had no history of any joint diseases. This joint disease developed after the implantation of 200 mg. of desoxycorticosterone acetate. When treatments with cortisone were reinstituted (25 mg. daily) the arthritis disappeared, and when the cortisone dosage was dropped to 12.5 mg. daily, the joint manifestations reappeared in mild form. It was necessary to maintain the dosage at 25 mg. daily to control the joint symptoms completely, although to all appearances 12.5 mg. daily was sufficient to control the adrenal cortical hypofunction, and on this level the symptoms of arthritis were minimal. That this case represents a definite correlation between arthritis and desoxycorticosterone acetate administration may be problematical. Since the patient had no symptoms of arthritis before treatment, however, I do not believe this was an aggravation of a preexisting disease. It may have been coincidental that the arthritis occurred with the administration of desoxycorticosterone acetate, although it was possible to control the arthritis by reinstituting cortisone therapy.

Student Detachment, Walter Reed Army Medical Center, Washington, D. C.

3. Thorn, G. W.: Studies on Adrenal Cortical Functions in Man, in The Recent Progress in Hormone Research: The Proceedings of the Laurentian Hormone Conference, edited by G. Pincus, New York, Academic Press, Inc., 1953, vol. 8.

4. Bauer, W., and Clark, S.: The Adaptation Concept in Relation to Connective Tissue Disease, in The Recent Progress in Hormone Research: The Proceedings of the Laurentian Hormone Conference, edited by G. Pincus, New York, Academic Press, Inc., 1953, vol. 8.

5. Haydu, G. G.: Rheumatoid Arthritis Therapy: A Rationale and the Use of Chloroquine Diphosphate, Am. J. M. Sc. **225**: 71 (Jan.) 1953.

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7. Ellman, P., and Cudkowicz, L.: Comparative Effects of Cortisone, ACTH, and DOCA in a Case of Rheumatoid Arthritis with Addison's Disease, Ann. Rheumat. Dis. **11**: 225 (Sept.) 1952.

SPECIAL ARTICLES

DRUG-INDUCED MOOD CHANGES IN MAN

1. OBSERVATIONS ON HEALTHY SUBJECTS, CHRONICALLY ILL PATIENTS, AND "POSTADDICTS"

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and
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The importance of the subjective response in the clinical use of certain drugs is such that the staff of the anesthesia laboratory of the Harvard Medical School has for some years been interested in the quantitative evaluation of these responses in the necessary experimental animal, man. Certain agents of considerable interest in pharmacology, such as amphetamine, may be used primarily to alter mood. On the other hand, mood changes present limiting factors in the use of some drugs

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Dr. John Spellman of the Holy Ghost Hospital, Cambridge, Mass., and Dr. Harris Isbell, of the U. S. Public Health Service Hospital, Lexington, Ky., cooperated in obtaining much of the data presented.

(e. g., euphoria and addiction liability in analgesics or dysphoria as an undesirable side-effect of any drug). We have found, in studying drug effects of this kind, that a combination of self-scoring questionnaires and interrogation is most successful in eliciting subjective responses from young, intelligent, healthy male volunteer subjects. In a pilot study of nine such subjects, the results obtained with morphine, heroin, and amphetamine were considerably at variance with textbook descriptions. It was therefore decided to amplify the questionnaire and to obtain written descriptions of effects (in the subject's own words), with comparisons of the various agents used by each subject. These experiments were repeated in 20 additional subjects. The results were comparable to those obtained in the pilot study. This report is concerned with these results in 20 healthy young subjects and with analogous experiments performed on a group of 30 patients, chosen to provide an experimental population that differed greatly from the first group in being chronically ill, old, hospitalized, and surrounded by the dying, and on a group of 30 "postaddict" prisoners at the U. S. Public Health Service Hospital, Lexington, Ky.

METHODS

Normal Subjects.—The subjects of the first group were 20 healthy male subjects, 21 to 27 years of age. They were told to refrain from drinking alcohol and to get a good night's sleep prior to experiments. At least 24 hours elapsed between experiments. Drugs were administered by a physician who was not involved in the evaluation of the effects. All medicaments were administered subcutaneously, with the exception of pentobarbital sodium, which was given intravenously. All subjects received sodium chloride solution (1 ml.) and amphetamine sulfate in a dose of 20 mg. per 70 kg. of body weight. The other three drugs were given at two dose levels, about half of each group receiving the higher dose of an agent and half the lower. These drugs and doses were: pentobarbital sodium, 0.05 and 0.1 gm.; heroin hydrochloride, 2 and 4 mg.; and morphine phosphate, 8 and 15 mg. All doses in this paper refer to the salts. For the sake of brevity, amphetamine, heroin, morphine, and pentobarbital are used in place of the salts. All medicaments were identified by code, so that neither the subjects nor the technicians were aware of the nature of the medicaments involved. The order of administration was random. During the entire testing period the subjects could be observed through a one-way window. The subjects were lying down or sitting during the experimental period and were allowed to read but not to smoke.

The status of each subject was determined prior to injection and at 30 minutes, one hour, and two hours after administration of the agent. For this purpose, a self-scoring questionnaire with 54 items was devised. Each item consisted of a pair of opposites, such as "sad . . . happy," or "practically asleep . . . wide awake," with a scale of seven possible degrees—a central zero point and three points on either side, as follows:

Sad						Happy
3	2	1	0	1	2	3

The items contrasted in the questionnaire and rated as "sad—happy" are as follows:

Shaky—serene; restless—peaceful; completely awake—practically asleep; things around me seem normal—everything seems unreal and dream-like; I hate everybody—I love everybody; I think this medication would help me a lot—this medication is the last thing I would want; physically energetic—physically lazy; very clear-headed—very groggy; right now if I had to memorize, it would be very easy—right now if I had to memorize, it would be impossible; sober as a judge—feel "high" as a kite; I feel extremely confident of my abilities—I have absolutely no confidence in my ability; this medication has had absolutely no effect—this medication has produced a striking change; I feel optimistic—I feel pessimistic; easy to concentrate—hard to concentrate; very nervous—calm; feel very serious—amused; apprehensive—confident; enthusiastic—apathetic; feel superior to my associates—feel inferior to my associates; people tend to underestimate me—people tend to overestimate me; I don't want to talk—I want to talk; cross, mad, angry—contented and friendly; I would very much like to repeat this particular medication—I wouldn't like to go through this again; if I couldn't sleep, I think this medication would help a lot—if I couldn't sleep, this medication is the last thing I would want; peppy—lethargic; senses very dulled—senses very acute; I'm very much interested in what's going on—I don't give a damn about anything; sad—happy; feel as if I've lost control—in complete command of myself; got the blues—cheerful; very uneasy—very much at ease; depressed—exhilarated; I want to be alone—I feel sociable; feeling of heaviness—buoyant; mind blank, difficult to think of anything—mind working like a dynamo.

General topics covered in the questionnaire were: thinking and concentration, mood, degree of wakefulness, and physical effects, such as palpitation, nausea, or dizziness. At the conclusion of the experiment, the responses were checked with the subject so that any qualifying remarks or additions could be recorded. At this time, also, each subject was asked to write, in his own words, a description of the effects of the drug. In some instances, observations were continued over a number of hours because of persistent effects. Any delayed effects were elicited by questioning on the next day experiments were performed. At the end of the five experiments in which a subject participated, he was asked to rate the five drugs as to order of pleasantness or unpleasantness. Any objective evidences of drug effect (behavior, appearance) were recorded by a technician.

Ten of the subjects were given one or more of the drugs in the original dose a second time, after the completion of the initial five experiments. In addition, 11 of the subjects received one or more of the medicaments (after the initial series of five) in different dosage, e. g., heroin, 1 mg.; morphine, 4 mg.; amphetamine, 10 or 30 mg.

Patients.—Thirty patients in a chronic disease hospital (Holy Ghost Hospital) were used as a second experimental group to provide a subject pool different from that of the normal volunteers. These patients ranged in age from 45 to 87 years. Twenty-two were men and eight women. Twenty-two of the group were hospitalized for malignant disease, with or without obvious metastases. The others had neurological diseases (multiple sclerosis, hemiplegia, paraplegia, muscular atrophy). Seven of the patients had occasional pain; five had fairly constant pain. If a patient was receiving a medicament "around the clock" for pain, this was not interrupted. The experimental medicaments were all administered

at the same time of day by a physician. The route of administration was like that in the normal volunteers except that pentobarbital was given intramuscularly. The doses used were: amphetamine, 10 mg.; morphine, 8 mg.; heroin, 2 mg.; pentobarbital, 0.1 gm.; and placebo (sodium chloride) 1 ml. These medicaments were administered in random order. Since many of the patients in this study were (because of age, physical condition, or mental condition) unable to make out the questionnaire satisfactorily, it was decided to obtain an evaluation, based on the responses of the patient to a series of standard questions as well as on the patient's behavior, as to whether a drug was pleasant, unpleasant, or neutral in its total effect. This evaluation was made in all cases by the same technician, who, like the patients, was unaware of the nature of the medicaments. In addition, the patients were asked to rate the five drugs in order of pleasantness or unpleasantness.

"Postaddicts."—Thirty "postaddicts" were studied at the U. S. Public Health Service Hospital, Lexington, Ky. This group included white and Negro subjects in equal numbers. This experimental sample differed from the entire hospital population at Lexington in at least several important respects. 1. The subjects were considered "incurable" addicts because of demonstrated recidivist tendencies. 2. They were volunteers. 3. They were "close" to drugs (including narcotics) because of participation in research in the recent past. No subject had been more than a week without a narcotic of some sort. A few had had narcotics as recently as two days prior to the start of the experiment.

The subjects were studied in groups of seven or eight. After preliminary instructions, they were asked to fill out questionnaires. These questionnaires were almost identical to the ones used by the normal subjects, except for the omission of items dealing with physical effects. A drug was then injected subcutaneously and the questionnaires made out again at 30, 60, and 120 minutes after injection. At the end of 120 minutes, the subjects were also requested to write down their reactions to the drug in their own words. The next day they were interviewed to ascertain whether they had experienced any delayed or persistent effects. A different injection was given each day for four successive days. These injections were administered at random in "double-blind" fashion. The subjects were not aware of the code numbers used, so that discussions with each other about drug effects at any time could not be oriented about a particular number. The subjects were told only that the drugs they were to receive were in no way new or untested drugs. They were allowed to sit together, read, or play cards. At some times a radio or television set was in operation. Conversation, smoking, and walking were not limited. Each subject was allowed to eat a regular meal (either breakfast or lunch) an hour or so before receiving each injection. In some instances these meals were missed because of anorexia or tardiness. Each subject received all injections at about the same time on the various days on which experiments were made.

About half of the experimental group (half white and half Negro) received the following medicaments: placebo (sodium chloride solution), heroin (4 mg.), morphine (15 mg.), and amphetamine (20 mg.). All of these doses were given per 70 kg. of body weight. The other half of the experimental group received one and one-half times the above doses, i. e., 6 mg. of heroin, 22.5 mg. of morphine, and 30 mg. of amphetamine per 70 kg. of body weight, plus a placebo.

RESULTS

Normal Subjects.—The effects produced by injecting 1 ml. of sodium chloride solution subcutaneously in normal subjects were, for the most part, unimpressive. Five of the 20 subjects had absolutely no effects, and another 9 had slight effects, which they attributed to sitting quietly and reading. These reactions were primarily sedative in nature ("less energetic," "slightly sleepy," "slightly lazy") and in all instances were felt to be due to environment and not drug. A typical comment was: "I don't believe I got any medication." None of the above 14 subjects considered the placebo either pleasant or unpleasant. The remaining six subjects had definite changes that they seemed to attribute to the injection. Five had mildly pleasant reactions ("slightly happier," "a little high," "more contented"), and one person had a mildly unpleasant reaction ("headache, groggy, less contented, shaky, confused"). Only one of these "placebo reactors" listed the placebo as the most pleasant drug of the five he received, and this was because all the others were either neutral or unpleasant. The person who considered the placebo unpleasant considered three other drugs more unpleasant. The incidence of physical side-effects was low after placebo (table 1), the most frequent being dry mouth, salivation, and a feeling of cold. Some of the subjects attributed the salivation to hunger and the "cold" to the fact that the experimental rooms were air conditioned.

Amphetamine: Amphetamine was outstanding in its ability to create a pleasant state. Thirteen of the 20 subjects listed amphetamine as the most pleasant drug of the five they received. In a number of instances these subjects spontaneously commented on how much more pleasant it was than the drug that they had listed as second most pleasant. Two other subjects listed the drug as second most pleasant of the series. In contrast to the case with all other medicaments, no subject felt neutral about the drug. The five subjects who did not consider the drug's effects pleasant all considered it unpleasant, two listing it as most unpleasant. Of this group of five, one subject found all the drugs unpleasant except pentobarbital, which he found neither pleasant nor unpleasant. Another found the initial experience quite pleasant but disliked the secondary effects. Samples of the descriptions by the subjects follow:

(D. S.): I began feeling very happy and enthusiastic. I began to read faster. I then switched to my French translating book and got quite enthusiastic over the stuff. My mind was clear enough, but I felt I didn't have complete control of myself. I was definitely "high." I felt a warm numbness and there seemed to be a coating over everything that would make bodily aches impossible. It was like being padded from external influences—as if wrapped in a blanket. [The technician described the subject as "tense, jumpy, and restless, yet easily amused, talkative."]

(J. C.): The most striking effect occurred very soon after medication. Suddenly my body felt light and I became very happy, indeed, exhilarated. This new state filled me with excitement and joy. A delightful drug!

(P. L.): An "all-over" good feeling. I felt capable of doing almost any task (within reason; at least I felt I could make a darned good try at accomplishing almost any task), and I felt confident of my abilities, not only for the present time, but also for the future. . . . The drug is a good "pick-me-up."

(H. M.): The medication took no effect for perhaps 10 minutes. Then I began to feel a deep sense of well-being come over me and a feeling of control over myself and confidence and power. I feel similar to when I'm playing the piano at my best . . . a feeling of exhilaration and satisfaction, not unlike the feeling that accompanies sexual satisfaction. All feelings of inadequacy or depression that I've felt at other times seem remote and trivial.

(I. I.): I became very, very happy with the world and its contents. All my previous tiredness and worry vanished completely, and I found extreme delight in reading a play I had heretofore frowned on. I became completely wrapped up in it and felt that I myself was enacting it. I felt as though I could transport myself to any clime or place and take up the habit assigned to me with perfection. I was joyful to an extent most uncommon and gratifying. I was so anxious to express myself that I babbled. Nothing disturbed nor lessened my feeling of confidence and power. . . . Each time I read a powerful line (and this meant every other line) I shivered (with pleasure?). The elation was in no way connected with that occasioned by liquor. Thanks for the lift.

(F. C.): The most impressive thing about it was the peaceful, "wanting to be alone" and undisturbed sensation. I felt more acutely aware of things, completely awake and able to concentrate clearly.

(P. T.): A quite sudden feeling of intense well-being, pleasantness, optimism, never felt better. Felt like singing. Have undue amount of optimism for future that I imagine will unfortunately leave me soon.

(T. M.): Hands shaky, very nervous, heart pumping. Seem to be forcing myself to increase the effect of thinking. My mind was working rapidly, thinking thoughts of action, conflict. Felt I could do anything, including lecture. Then I found I could hardly talk. The experience was interesting and exciting. As it began wearing off, I became angry that it hadn't lasted longer. [The technician's observations were: "Twenty minutes after drug, subject appeared very tense and afraid. His expression was one of anxiety. He was sitting looking at a lamp and gripping the chair with both hands. He seemed relieved to see someone to talk to but also seemed reluctant to talk."]

(G. G.): I became optimistic and any troubles I had seemed easily soluble, but I had a feeling of tenseness that increased with time and dissipated the optimism. This gave way to a nameless anxiety that made me uncomfortable and even fearful.

In regard to mentation and degree of wakefulness, amphetamine was described as depressant almost as frequently as it was stimulant. Thus, 12 subjects actually felt more alert, while 8 felt sedated. Similarly, eight subjects described themselves less able to concentrate or read. Physical effects are listed in table 1. Shakiness, dry mouth, palpitation, and paresthesias were frequently described.

Heroin: Heroin was given at two dose levels. Eleven subjects received 4 mg. per 70 kg. of body weight. Seven found this dose unpleasant, with one of these, however, finding it initially slightly pleasant. Sample descriptions follow:

(L. E.): I felt irritable, shaky, unsteady, and nauseated. Angry at doctor for making me sick. [The technician observed: "Coarse tremor when moving hands. Sighing. Very pale, perspiring."]

(J. C.): Very shortly I felt quite dizzy and my calm and happy disposition when I came in soon disappeared. I felt rather sad, melancholy, rather nauseated throughout. It was hard to concentrate but I could not relax. All in all a rather unpleasant experience.

(M. P.): The first feeling was a tingling sensation, then an inability to focus on anything. This was accompanied by neither a happy nor a peaceful feeling, but just a willingness to allow the effects of the drug. Movement of the body caused dizziness and nausea.

(I. I.): The major effects began almost immediately and consisted of dizziness and inability to concentrate. This decrease in ability to focus on a problem and analyze it adequately led to a period of distress and then irritation.

(M. B.): Slight dizziness, loss of control over my speaking faculties, a feeling of warmth. Somewhat later, I began to burp and hiccup. At this point, a noticeable lassitude set in.

Two of the subjects felt that the medicament had been neither pleasant nor unpleasant. One asked whether he had received a medicament at all, and the other considered the only effects to be physical ones (itching, hiccups, sleepiness, lethargy). Two of the subjects considered the effects pleasant, although each subject considered them less so than those produced by amphetamine:

(K. H.): Medication caused me to feel dizzy and dulled my sense of hearing. I felt a little glow and sense of satisfaction with the state of things. The chief effect—and it was not marked—was a not unpleasant dizziness.

TABLE 1.—*Incidence of Physical Side-Effects in Twenty Normal Subjects*

			Pentobarbital		Heroin		Morphine	
	Placebo	Amphetamine	0.1 Gm.	0.05 Gm.	4 Mg.	2 Mg.	15 Mg.	8 Mg.
No. of subjects	20	20	12	8	11	9	11	9
Headache	2	3	4	1	4	2	6	3
Nausea	1	5	4	1	6	3	6	3
Dizziness	1	7	9	6	10	3	9	7
Shakiness	..	8	..	..	6	3	7	2
Tingling and numbness	1	9	3	2	6	2	7	4
Itchiness	2	2	..	..	6	4	5	..
Dry mouth	3	9	..	..	4	3	6	4
Salivation	4	1	2	1	3	1	..	..
Warm	1	4	..	..	5	3	6	3
Cold	5	6	5	5	2	2	..	1
Palpitation	..	9	..	..	2	1	2	1

(F. C.): About two or three minutes after the medication, I felt a slight swimming in my head. Soon it became an over-all very pleasant sensation of warmth. Made me just want to close my eyes and sit back and feel good. Very pleasant.

In all subjects, the effect on mentation and state of wakefulness was described as a depressant one. Dizziness, nausea, warmth, tingling, and itchiness were common side-effects. Shakiness (despite sedation) occurred in six subjects.

Reduction in dosage of heroin seemed to lower the incidence of dysphoric reactions and increase the percentage of persons experiencing few or no effects. Thus, of the nine subjects who received 2 mg. per 70 kg. of body weight, only three found the drug unpleasant:

(D. S.): I lost interest or at least the ability to concentrate. My mind wandered freely and I had to force myself to stay awake. I felt a slight heaviness in my head. No emotional changes, but the whole experience was mildly unpleasant.

(W. H.): Dizzy, tense, mentally confused (unpleasant) slowness, feeling of not wanting to think (blank feeling), irritable.

(A. G.): Hot, dizzy, heaviness in arms and legs; sleepy, slightly shaky.

Three of the subjects found the experience pleasant, two of them very slightly so:

(T. M.): I feel as if I would like to have had a dose twice as powerful. Almost immediately my head began to feel buoyant. It made me lazy, too dizzy to read fine print. Gave me a general feeling of contentment. Generally, it was very pleasant.

(P. T.): Very little effect. Felt glowy and enthusiastic for about 30 minutes. Was dizzy for a short while. Practically no effects, but I suppose you would call it very slightly pleasant.

(T. N.): The medication made me experience a sort of peaceful, comfortable feeling from 10 minutes after injection until 40 minutes after. Itchiness also started after 10 minutes and still persists now [after two hours]. Peaceful feeling replaced by drowsiness. I have not been as hungry as I usually am. The whole thing was a feeling such as you'd get from sitting in front of a fire if you're tired.

The other three subjects considered the experience neither pleasant nor unpleasant.

(H. P.): A slight tingling in my fingers. My emotional attitude did not change in any way.

(W. R.): Neither pleasant nor unpleasant. Slight relaxed warm feeling.

(R. H.): A giddy, "heady," semianesthetized feeling—all wore off in 45 minutes. Pleasant only if you consider a new experience pleasant.

The physical effects, like the effects on mentation and wakefulness, were less marked but similar to those described above for 4 mg. of heroin.

Morphine: Morphine was also given at two dose levels. The effects of 15 mg. were predominantly unpleasant. Of the 11 subjects who received this dose, 8 considered it the most unpleasant medicament of the series of five. Six of these 11 subjects considered the experience unequivocally unpleasant from the beginning to end:

(L. E.): Feel very dizzy and not in any way capable of doing anything physical or practically anything involving deep concentration or mental application.

(F. C.): Just after medication was given, I began to feel a bit nauseous and a dizziness in my head. Stomach feels uncomfortable. I have to squint to keep my eyes open and from burning. Can't concentrate. Feel generally uncomfortable and shaky. Mouth dry. I feel tired and grouchy. [The technician observed: "Became very pale and droopy-eyed."]

(M. B.): After about five minutes a tightness in the circulatory passages of my head set in. This made me feel warmer there and was combined with a slight tingling sensation. Slight itchiness and drowsiness and dizziness set in, with an inability to read without losing my point of focus. Suddenly I began to have the hiccups, and the drowsiness immediately disappeared.

(P. L.): Eyes and head heavy. A little nausea. I got the shakes about 10 to 12 minutes after the injection. Heart is beating a little harder. If effect went any further, it would be very irritating and would no doubt give me the jumps and might make me throw up. [Vomited later.]

(G. G.): Dizzy, nauseous, headache, feel warm. Vomited. Difficulty focussing my eyes. Headache very bad.

(J. C.): Dizzy, arms and legs heavy. Head especially heavy and thick. Very sleepy. Later, I felt very nervous (shaking all over) and cold.

The other five subjects also considered the total experience unpleasant but had transient initial (four subjects) or secondary (one subject) pleasant effects of a mild nature:

(M. P.): The first effect was a tightening of the jaw region. Then a slight tingling sensation of the body and a slight feeling of relaxation and serenity. Mind does not seem to be too effectual. I have not enough motivation to concentrate and read anything difficult. Would rather lie back and relax. Later, a slight feeling of nausea, with loss of feeling of optimism. Very dizzy. Feel lousy and sleepy.

(K. H.): I first felt relaxed and dizzy, sleepy, and weak in the stomach. These late effects were quite unpleasant.

(A. M.): A transient slight release of tension early in the experiment, followed by unpleasant headache, dizziness, nausea, dry mouth. Final effects were depression, shakiness, irritation.

(H. M.): Numb and slightly dizzy. Reading very slowly. My senses feel dulled, and there's a numbness in my head. Late effect was a diffuse itchiness. Urge to act as if drunk. Feeling that I've been doped. Numbness finally gave way to a mild "high" feeling. Pleasant sense of well-being like that experienced in first experiment [pentobarbital].

(I. I.): The initial reaction began about 15 minutes after the injection. First my ears had the same feeling that one gets when atmospheric pressure undergoes a rapid change. My chest felt compressed. Head became dizzy, and I found difficulty in focussing my mind. I felt somewhat elated and relaxed—somewhat euphoric, as after a beer or two; an absence of worry and satisfaction with the world. Arms felt heavy. Head became dizzier, arms and legs heavier. I could detect an itching in several parts of my body. Although relaxed, tired, and sleepy, my hands were shaky—mentally relaxed, yet physically unstable. The later effects were feelings of grouchiness and irritability, making the whole experience unpleasant, although initially it was pleasant.

The effects on mentation and state of wakefulness were depressant in all cases. The physical effects were quite marked, with dizziness, nausea, dry mouth, tingling, headache, warmth, and itchiness being prominent. Of interest is the shakiness described by seven of the subjects.

As in the case of heroin, decreasing the dose of morphine by half produced a lower incidence of unpleasant reactions and a higher incidence of neutral reactions. Three subjects found 8 mg. pleasant, although the late effects in one case were sufficient to make the subject's final estimate of the drug unpleasant.

(D. S.): I felt tired, sleepy, logy, relaxed—I would have been very happy to curl up and go to sleep. This drug would not be good for a psychotic depression but would tend to decrease something like business worry. [After going home, subject "felt at peace with the world. I looked in the mirror and my eyes were only half open. I went to sleep right after supper."]

(W. H.): After the initial effects of stomach upset and scattered pains, it was a very pleasant drug, producing a great sleepiness, a feeling of calm and contentment. There wasn't at any time a fuzziness of thinking. It was like being drunk without any of the unpleasantness of mental fuzziness.

(R. H.): Fifteen minutes after injection I experienced a sensation not unlike that brought on by drinking liquor. A quarter of an hour later the sensation lost its effervescent quality and was transformed into a heavy dulness. Got nauseated much later in the evening.

Two of the subjects considered the drug neither pleasant nor unpleasant:

(T. M.): There isn't any good feeling from this drug, only a pressure on the head and back of neck, and a feeling that my pulse and respiration are faster than usual.

(T. N.): I didn't feel anything at all, except that my left arm was sore for about 20 minutes.

The last four subjects considered the drug unpleasant:

(H. P.): The results of this drug were completely mental. A rather serious mood and disinterest in people seemed to result from the medication. Nothing unpleasant other than that.

(A. G.): Felt hot and dizzy and lethargic. These sensations and a dulness were slightly unpleasant. [The technician observed: "Face became flushed. He looked tense and worried. Perspiring freely."]

(W. R.): Dryness and tightness in throat, slight dizziness. Headache and watery eyes. Breathing seemed difficult and eyes were heavy.

(P. T.): Felt sleepy after about 10 minutes, with a slight moodiness, on the blue side. Didn't feel like talking or seeing anyone. Got quite sleepy and dozed off for 10 minutes. Had trouble concentrating.

The effects on mentation and wakefulness and the physical side-effects were similar to those observed with 15 mg. but were less marked.

Pentobarbital: Twelve subjects received 0.1 gm. and eight subjects 0.05 gm. of pentobarbital intravenously. Although there was a quantitative increase in the subjective changes with the larger dose, the similarity of effects at the two dose levels studied seems to warrant discussing all 20 subjects as a single group. The primary effects of this drug were sedative in nature. All but three of the subjects felt sleepy at some point. The other major effect, present in six of the subjects, was a transient "high feeling," occurring right after injection and consisting of giddiness and an associated euphoria, frequently associated with spontaneous grinning or laughter and occasionally associated with dysarthria. This state was frequently compared by the subjects with "a quick drunk." The drug was considered pleasant by nine of the subjects, unpleasant by five, and neither pleasant nor unpleasant by six. In no instance did a subject feel strongly enough about his reaction to rate it either most pleasant or most unpleasant. Typical descriptions follow:

(P. T.): As the medication was being injected, I felt a sharp and sudden dizziness and a general lethargy of senses and limbs. I could hardly lift my eyelids. I felt sleepy and was continually dozing off. I still feel sleepy and lethargic now, after two hours.

(K. H.): I felt "high"—a glow like being a little drunk. Then I got sleepy.

(P. L.): The drug took immediate effect. My head got heavy. I got a tremulous "high" feeling and was generally sleepy. The drug gave me a highly amusing feeling and one of light-heartedness. I felt sociable but couldn't help but wander off to sleep. For a short time I felt the same as when I get "high" from an intoxication. It made me feel "good" all over.

(D. S.): A feeling of haziness—not unpleasant. Later, a depressing feeling, like a "hangover."

Comparison of Drugs on Basis of Questionnaire: A comparison of the drugs was also made on the basis of the responses to the questionnaire. A score was compiled for each subject for each drug on the following major classifications in the questionnaire: mood, mentation, and sedation. These scores were derived as follows: Mood was covered by 19 items in the questionnaire. Examples of these items are: "optimistic . . . pessimistic," "serious . . . amused," "irritable . . . contented," "sad . . . happy." For any one item there were three occasions when the postdrug state could be compared with the predrug state (one-half, one, and two hours after medication). The units of change at each of these checks were added together algebraically to obtain a score (+ for euphoric, — for dysphoric) for the item, and then all the scores for the 19 items were totaled and a mean score derived. For example:

	Sad						Happy
Predrug	3	2	1	0	**1**	2	3
½ hour	3	2	**1**	0	1	2	3
1 hour	3	**2**	1	0	1	2	3
2 hours	3	2	1	**0**	1	2	3

The score for this item would be —2 on the one-half hour check, —3 on the one hour check, and —1 on the two hour check, adding up to a total of —6 for this particular item, a dysphoric score. If the mean score for all 19 items was on the positive side, the patient was classified as having had a euphoric reaction to the drug; if on the negative side, it was called a dysphoric reaction. These mean scores for all 20 subjects were added algebraically and a group mean score for each drug derived, which again was labeled euphoric or dysphoric according to sign. Sedative effects were similarly assessed, with the use of the six items in the questionnaire dealing with the state of wakefulness. Sample items in this group are: "peppy . . . lethargic," "wide awake . . . practically asleep." Effects on mentation were calculated from the seven items dealing with this general topic. Items in this group included: "very clear-headed . . . very groggy," "easy to concentrate . . . hard to concentrate," "senses dulled . . . senses acute."

TABLE 2.—*Questionnaire Scores on Mood Items in Twenty Normal Subjects*

	Euphoric		Dysphoric		Group Mean Score	
	No.	Mean Score	No.	Mean Score	Euphoric	Dysphoric
Placebo	6*	23	8*	8	4	..
Amphetamine	14	43	6	30	21	..
Pentobarbital	9	14	8	12	2	..
Heroin	9	18	10	34	..	9
Morphine	8	16	10	44	..	16

* In tables 2, 3, 4, 7, 8, and 9, the subjects not accounted for in a particular line had scores of zero. Thus for placebo, 6 subjects had euphoric scores, 8 had dysphoric scores, and 6 had scores of zero. The group mean scores include all subjects in the particular experimental group (20 in this table).

TABLE 3.—*Questionnaire Scores on Sedation Items in Twenty Normal Subjects*

	Sedated		Stimulated		Group Mean Score	
	No.	Mean Score	No.	Mean Score	Sedated	Stimulated
Placebo	11	12	3	4	6	..
Amphetamine	9	11	9	13	..	1
Pentobarbital	17	20	3	6	16	..
Heroin	17	16	1	1	14	..
Morphine	18	18	..	..	16	..

TABLE 4.—*Questionnaire Scores on Mentation Items in Twenty Normal Subjects*

	Impaired		Improved		Group Mean Score	
	No.	Mean Score	No.	Mean Score	Impaired	Improved
Placebo	11	7	2	4	3	..
Amphetamine	3	3	3	16	..	3
Pentobarbital	16	20	2	4	16	..
Heroin	18	19	..	..	17	..
Morphine	18	23	..	..	21	..

These results are given in tables 2, 3, and 4. The scores on mood, mentation, and sedation corroborate, in general, the final evaluation by the subjects. Thus, amphetamine stands out in the production of euphoria, with a mean score of 21 (table 2), while morphine has the highest dysphoria score, 16. The discrepancies between number of patients listed as euphoric or dysphoric in this table and in previous sections in this paper are explainable on four counts: 1. A person was listed as euphoric even if his mean score for the mood items was +1 (and dysphoric if —1). Such minor changes were frequently attributed by the subjects to "merely sitting around." 2. The questionnaire covered only the first two

hours, whereas occasionally reactions of a type dissimilar to the original ones occurred or reached their peak after this time. 3. The questionnaire scores do not take into account qualifications and amplifications made by the subjects at the end of the experiment. Such statements occasionally altered the meaning of the questionnaire responses. 4. All items were considered equally in calculating the mean scores, although a particular patient may have considered some changes more important than others in determining pleasantness or unpleasantness. Similar considerations apply to the analyses for mentation and sedation. An item on the questionnaire that was tabulated separately was: "Would like to repeat, even without pay . . . I wouldn't go through this again for anything." The results are given in table 5.

Repeat Tests: As a check on the consistency of response, 10 subjects received one or more of the five drugs a second time, in identical dosage, after the completion of the five experiments. The fact that these were repeat experiments was of course not divulged to the subjects. Eight subjects received a second injection of sodium chloride solution. Three subjects who had previously had a slight pleasant reaction from the placebo

TABLE 5.—*Responses of Normal Subjects to Questionnaire Item on Repeating Drug Experience*

	Would Like to Repeat	Would Not Like to Repeat	No Feelings One Way or the Other
Placebo	3	1	16
Amphetamine	14	2	4
Pentobarbital	3	3	14
Heroin	4	7	9
Morphine	2	9	9

felt this way again the second time. A fourth subject had slight sedative effects both times. The subject who originally considered the placebo unpleasant had no reaction the second time. Three subjects who did not have any reactions the first time also experienced no effects the second time. Three subjects received amphetamine (20 mg.) a second time. One subject (T. M.), who originally found the drug "interesting and exciting" but rated it unpleasant, had a "very pleasant" reaction the second time, with a "touch of nervousness." K. H. found the drug pleasant on both occasions, with almost exact repetition of symptoms. H. P., who found the drug "depressing" and sedative the first time, had exactly the same reaction the second time.

Four subjects had repeat doses of morphine. D. S., who originally had a pleasant, sleepy, relaxed feeling, had the same reaction initially the second time but later on became nauseated, dizzy, and felt "terrible." T. M., who felt slight sedative effects, headache, and tachycardia on the initial exposure to morphine, felt identical reactions the second time. He commented: "I had this medication before." P. T., who had considered the drug slightly unpleasant the first time and had felt somewhat sleepy, described his second experiment as producing no mood effects, "just dizzy and sleepy." The last subject, M. B., considered the drug unpleasant on both occasions, the only difference being actual vomiting the second time, in contrast to nausea on the first experiment. Three subjects received repeat doses of heroin. These persons had essentially the same reactions as in the first trial (one "unpleasant," two "slightly pleasant").

Experiments with Different Dosage: Eleven subjects received (in addition to the standard doses described above) one or more of the drugs used in the study in either higher or lower dosage. Seven subjects received 10 mg. of amphetamine per 70 kg. of body weight. Four of these, who had considered 20 mg. of this drug the most pleasant medicament of the group of five in the original series, also considered this smaller dose pleasant, but the effects were much less marked. A fifth subject found the smaller dose only mildly sedative. The last two subjects (T. M. and G. G.), who originally rated the drug as unpleasant because of unpleasant side-effects, found the smaller dose pleasant. Five subjects received 30 mg. of amphetamine per 70 kg. of body weight. One of these (H. M.) considered it very pleasant, stating, "I wish I felt like this 24 hours a day." The other four, who had considered 20 mg. of this drug pleasant, found that the euphoria induced by the larger dose was marred by such side-effects as palpitation, jitteriness, and dizziness.

Five subjects received 1 mg. of heroin per 70 kg. of body weight. Four of these had only slight sedative effects that were neither pleasant nor unpleasant, whereas three of them had originally considered the drug (in 2 or 4 mg. dose) pleasant. The fifth subject, who had found 4 mg. unpleasant, found this smaller dose equally unpleasant. Four subjects received 4 mg. of morphine per 70 kg. of body weight. Three had essentially no effects of any kind, whereas all of them had considered at least some of the effects produced by 8 or 15 mg. of the drug as pleasant. The fourth subject described the effects as insignificant except for some depression of mentation and some sedation and "for 10 minutes (after almost two hours) I felt a pleasant relaxed sort of glow just when I thought the drug had worn off."

Patients.—The 30 chronically ill patients had responses that could be characterized as "feeling happy" (or "happier"), "unpleasant effect," pleasant effect in that symptoms were relieved, "made me feel stronger," "sleepy," and no change. These results are given in table 6. When asked to rate the drugs in order of pleasantness, six patients did not seem to remember well enough to compare the five drugs. Eight felt that there were no real differences between the five drugs. Of the 16 who did rate some drugs as more pleasant than others or more unpleasant, 4 picked amphetamine as best drug, 2 picked heroin, 3 morphine, 2 placebo, and one pentobarbital. Two patients considered morphine the most unpleasant drug, and one subject each considered placebo, heroin, and pentobarbital as most unpleasant. Of interest is the fact that a number of the patients spontaneously commented on a decrease in pain after administration of the medicament. Thus, two patients observed this after placebo, four after heroin, seven after morphine, and seven after amphetamine.

Postaddicts.—Twenty-one of the 30 postaddict subjects felt absolutely no effects at all after administration of the placebo. Nine of the subjects experienced effects to varying degrees. Four of these considered the total experience after placebo neither pleasant nor unpleasant;

four considered the placebo unpleasant, with three calling it the most unpleasant drug of the four received, and one considered the placebo pleasant. The reactions described were:

(Jo., B. L.): Got a queasy feeling in the pit of my stomach about 10 or 15 minutes after the injection. It lasted 5 or 10 minutes. Later [at night] it felt heavy in the pit of my stomach. I was restless and couldn't sleep until 4 a. m. This is very unusual for me.

(Fo.): My stomach got upset at night. I slept O.K. but was drowsy the next morning [unusual].

(Ba.): My eyes were heavy, but I was not sleepy. At night I got evil, like from LSD [*d*-lysergic acid diethylamide]. Didn't like to talk to anyone—never feel that way naturally.

(Gl.): Slept better than usual at night, with a very good appetite.

(Warr.): I seemed to be more awake after the shot. Seemed more easy to concentrate. Was very calm. Wanted to talk. Very contented. A little more peppy. Interested in things that were going on. Don't think it was an opiate. Slept very well at night. Usually have to get up three times during the night to urinate —last night I was up only once, at 4 a. m.

(Ol.): This medicine settled my stomach, made me a little peaceful and calm. I went to sleep in the afternoon, which is very unusual for me.

(We.): Slightly lazy and pessimistic. Have had something but results so slight I can't tell what it is. Had four bowel movements. Didn't like drug's effects.

(Bar.): A slightly depressed and lethargic feeling. Not a narcotic. Restless all night. Got up to urinate six times instead of usual one or two.

(Cr.): Effects very much like cocaine. It produced a very exhilarating feeling and made me feel a little wild. I would not care for this drug unless I had morphine to quiet me down after using it. Could not get any rest or sleep at night. Produced a feeling of being off a habit after 10 days. Made me antisocial. Would not care to take this drug for any length of time.

Amphetamine: As in the case of our normal subjects, amphetamine reactions were rarely described in neutral tones by the postaddicts. Only three subjects had no reactions at all, with five others considering the reactions neither pleasant nor unpleasant. Of the 14 subjects receiving 20 mg., 6 considered the drug pleasant, but only one of these called it the most pleasant drug of the four received. Four considered the drug the most unpleasant of the series, although one of these had an early reaction that was as pleasant as that from morphine (his "most pleasant" drug). Three subjects considered their reactions neither pleasant nor unpleasant, and one subject experienced no reaction at all.

The persons who called the drug pleasant had the following reactions:

(Si.): Very slight effect. Don't know what drug it is. Made my voice hoarse, like a drug would do. Would call it a mellow feeling.

(Bar.): In 10 minutes it caused a "high" feeling that commenced to subside after 30 to 40 minutes. At first I felt as if I had a shot of Demerol [meperidine]. This is because I have had no itching. Also I had a sweetish taste 15 to 20 minutes after the hypo. I am not hungry. I do not feel as energetic or as sociable and loquacious as I first felt after the shot. It made me feel talkative, buoyant, and "light." I felt "good," happy, and contented. (At night I felt pretty much of a let-down. Head like a balloon, with dull ache. No appetite at noon or supper—some nausea and nervous stomach. Dryness of mouth. Lips tended to crack and have slimy taste. Very nervous—could not rest. Leg muscles and bones ached from knees downward.

(Warr.): Feel like it was some kind of opiate. Equivalent to 1/16 grain [4 mg.] of Dilaudid [dihydromorphinone]. Very pleasant feeling.

(Hu.): At first I felt a very slight exhilarating sensation akin to morphine. If it was "M" [morphine] there wasn't enough of it to compare with any reasonably large dose I've had before. Like ⅛ grain [8 mg.] under the skin—but different because I felt clear-headed, with none of my usual sinus trouble. In that sense it's like Benzedrine [amphetamine]. Also easier to concentrate with this drug, which is different from morphine.

(Au.): I really received a nice feeling from the medication. It reminds me of some good cocaine—happy, nervous, and jumpy. I hope this feeling won't wear off too soon.

(Gl.): A peaceful feeling.

The subjects who considered the total drug experience unpleasant had the following reactions:

(We.): Feel I've had something not in the opium family unless it was codeine. Made me lose my appetite. No sleep at night —nervous.

(War.): Today I feel I had an injection of cocaine or something in that immediate family because of gritting of teeth, nervousness, and restlessness. [Very bad night—restless—"I think it must have been a large dose of Benzedrine."]

TABLE 6.—*Effects of Drugs in Thirty Hospitalized, Chronically Ill, Elderly Patients*

	Happy	Pleasant Only Because Symptoms Relieved	Stronger	Sleepy	No Change	Unpleasant
Placebo	10	..	3	5	12	..
Amphetamine	17	..	..	..	12	1
Pentobarbital	13	..	..	9	6	2
Heroin	11	..	..	6	10	3
Morphine	10	4	..	6	2	8

(Sm.): I felt very light in the head and a little groggy—lost my appetite. I would say about 1/4 or 1/6 grain [15 or 10 mg.] of Dolophine [methadone]. [After a night marked by lack of sleep and appetite, he decided it had been Benzedrine.]

(Cl.): It affected me first like morphine (stomach turned), then like codeine (because it didn't last) and finally like Benzedrine or Dexedrine [dextro-amphetamine]. It made me somewhat energetic and nervous, but was not at all unpleasant. [At night he slept only one hour, was very nervous, "miserable all night."]

Of the other four subjects, none considered the drug particularly pleasant or unpleasant; one (Go.) had palpitation but "no other unnatural feelings" and felt a little more talkative. He could not go to sleep at night, but instead lay quietly in bed, "concentrating on a lot of bygones." Another subject (Ol.) believed he had received "a derivative of cocaine or Benzedrine. I feel the drive of cocaine, also my mouth has an unpleasant taste. I also feel the tightness of my teeth, and the closeness of my throat, as if I can't swallow. When I urinated, I couldn't even feel my penis, and my water came very slow. No appetite. Slept very restless and woke up about four times." A third subject (Do.) felt only "a little calm and a pain in the stomach. At night I didn't sleep—restless, pain in the stomach, no appetite. My bowels moved a lot, and my penis shrank just like with Benzedrine." The last subject (Sh.) had no reaction at all.

Sixteen subjects received 30 mg. of amphetamine. Seven found this drug to be pleasant, five of the seven calling it the most pleasant drug. Five found the drug

most unpleasant, although one of these initially described it as pleasant. The other four subjects either had no reactions (two), or slight effects that were neither pleasant nor unpleasant (two). The seven pleasant descriptions follow:

(Gon.): At first I felt real good. My after-effect was something like cocaine. My cheeks felt like they were swollen. My sex nature felt funny, like I wanted to have a woman—just like I wanted my desires fulfilled. I also got a severe stomachache, and my head felt sort of funny. A slight headache. I enjoyed myself quite a bit. I didn't eat supper, breakfast, or dinner. Stomach hurt a lot. I woke up at 4:30 a. m. feeling real bad. Muscles hurt. Sneezing and little chills. About 10 a. m. I wanted a shot of dope real bad. I had a yearning, like I was hooked.

(Cr.): I feel as though I had eaten 40 mg. of Benzedrine tablets. It produced a pleasant sensation. I talked a good deal more than usual. It has made my mouth and nose dry. I would like to repeat this drug. [Did not sleep at night.]

(Wal.): Pleasant sensation similar to cocaine inhalation. Friendly and talkative—that's what drugs do to me. I'm not like that unless I take drugs. A little shaky at first and then rather calm. No appetite at night, and no sleep—a "let-down" feeling.

(Gr.): Very nice, very light feeling—more pleasant than with heroin or morphine. Strong effect but didn't linger at original peak. Terrible headache later [at night]. Very restless, hard to sleep.

(Ba.): I felt very contented and amused—like cocaine except not as nervous. No appetite.

(Fo.): A slight buzz. Felt good, sociable for about 10 minutes.

(Dy.): A little nervousness in stomach and a little lightness as if I could have gotten a kick out of it if it had been stronger. Didn't sleep at night.

The five unpleasant reactions were as follows:

(De.): Felt a mild, good sensation, like a small shot of dope, like a warm glow in the stomach, for four to five minutes. Felt like a mild dose of Benzedrine [20 mg]. Left me nervous and restless afterwards. Chills for hours. Excessive walking and talking. No appetite. Only slept one hour. Pupils dilated. Very nervous.

(Pe.): Nervous, shaky, I believe I got ½ grain [30 mg.] of cocaine.

(Da.): Twenty minutes after the shot my heart started beating faster. Could feel my flesh tightening over my body. Gave me a drive something like cocaine. Was restless, got no sleep at all. Would not like to repeat.

(Jo., J. W.): Something like cocaine. Awake, restless nearly all night.

(St.): Thirty minutes after injection I felt very apprehensive; fear and anxiety evident. Heart beating very hard. Uneasy as to outcome because I feel very peculiar. My head feels like it is being squeezed inside or brain tingling. A spot on top left center of head feels numb. Jaws and mouth feel peculiar. Eyes watering. Cold and chilly all over. Hands extremely cold. Yawning. Mucosa of mouth thick. Several extrasystoles. Hard violent pounding of heart—conscious of each beat. Feeling in chest of tightness and muscle tension. Peculiar sensation in solar plexus radiating out to other parts of body. Left arm weak. Fear of walking because of fear of passing out and shallow breathing. Sighing, as an aftermath of extreme grief. Sense of hearing dulled considerably. Sounds received belatedly, not acute. Lacrimation. Funny drawing sensation down inside of right thigh. Became talkative an hour or so after realizing the symptoms were not to be more severe. Anxiety subsided. Vacillation from fear to confidence. Some drug of narcotic type—very nice as an experiment but not for regular use. Had all the good feeling of narcotic without nausea. [Slept not at all at night. Mind very active—recalled a poem completely that he had not remembered for years. Wrote poetry. Despite above description, subject was very loquacious, laughed and talked to the other subjects. Told very funny stories. Said he'd had something "very, very good." Looked and acted "high as a kite."]

Four subjects considered the drug neither pleasant nor unpleasant. Two had no reactions at all, one felt only a "lump in the throat," and the fourth felt he had received something with stimulant qualities but "not a narcotic."

Heroin: Fourteen subjects received 4 mg. of heroin. Half of the group found the drug pleasant, although only one considered it the most pleasant drug of the series, and one considered it and morphine as tied for "most pleasant." Five of the other seven subjects felt no reaction at all, one only felt transiently dizzy, and one felt he may have had heroin, but "it was too slight a reaction to be sure." The pleasant reactions were as follows:

(War.): I believe I had about 20 mg. of morphine sulfate. I had a definite stomach rumble and a sort of jubilant feeling. It seemed to leave me in a hurry, like a shot of Dilaudid. If I were to repeat this I would like half again as much.

(Bar.): Believe the injection was about ¼ grain of morphine sulfate. While the euphoria has subsided somewhat, I am not yet nervous. I have little itching of the skin, which usually follows a sizeable shot of morphine, heroin, or Dilaudid.

(Gos.): A slight glow—just a touch of narcotic.

(Ol.): This is a narcotic—in the opiate family. Dosage can't be more than ¼ grain of morphine. Exactly the opposite effects of yesterday's drug [amphetamine]. Slept well at night, but woke up very tired. It was hard to wake me up.

(Sh.): Pleasant—hit me in the pit of the stomach and gave me a taste in the mouth. So slight I can't tell what it was.

(Hu.): Somewhat like a very small dose of heroin or Demerol.

(Do.): Felt cheerful, calm, relaxed, and confident of myself. Wanted to talk and be sociable. Also a little buoyant and amused. Later, I got pains in my stomach for about 20 minutes. Not reminiscent of anything I've ever had. Exactly the same as yesterday's reaction [morphine].

Increasing the dose of heroin to 6 mg. seemed to cause an increase in unpleasant reactions. Seven of the 16 subjects considered the experience pleasant, with 4 of the seven calling it the most pleasant drug of the series. Four of the subjects had no reaction at all. Two others considered their reactions as neither pleasant nor unpleasant; one had slight itching and extreme sleepiness the next morning; the other felt slightly shaky and did not sleep at night. The remaining three subjects considered the drug unpleasant, two of them calling it the "worst" medicament. The pleasant reactions were as follows:

(Jo., J. W.): Like a very small shot of Demerol (10 mg.)—slightly peaceful and friendly.

(Da.): Very clearheaded for one hour. Like a very mild narcotic.

(Ni.): Like very much to repeat this medication. Feels like ¼ grain of morphine or Dolophine. Clearheaded, easy to concentrate, friendly, talkative, peppy.

(De.): A very mild peaceful feeling and relaxation. Like a small dose of sedative.

(Cr.): Had a headache before the injection that immediately left. Very similar to yesterday's drug [morphine]. An opiate mixed with a stimulant of the cocaine family. The feeling is pleasant and desirable. I would like a stronger dose. I would judge this drug to be 1/32 grain [2 mg.] of Dilaudid, with a small amount of cocaine.

(Pe.): I had methadone today. Peaceful, serene, clearheaded, talkative, friendly.

(Jo., B.): I got a nice feeling followed by a slight itching and then a pleasant glow. Shaky for a little while. Friendly feeling toward everyone. Tasted sweet and cool on the tongue (like cocaine). My saliva ran free. Later I had cool spots running through my body (like morphine). Had a heavy head next morning, but my appetite was increased after I got the drug.

The unpleasant reactions were described as follows:

(St.): I was conscious first of a feeling of warmth over the upper part of my body and face. Became nervous, noted shaking of my arms and hands accompanied—as in all nervous situations—by dryness of the mouth and throat. I would not want to use this again. I would prefer pain or anxiety to this medication. I was perfectly oriented but possibly more aware of myself. I do not think I had an opiate, but reaction was similar to a small dose of Demerol except I did not have the taste of Demerol.

(Gr.): No effect for a couple of hours—then I got sick to my stomach but didn't vomit. Went to sleep at 6:30 p. m. Felt groggy and tired, like a drunken man. No appetite even on the next day. Never felt this way from any drug before. I did not feel "high," just bad.

(Fo.): No reaction until night time. I felt evil and depressed. Didn't want to talk. Didn't want to be bothered. Very unusual.

Morphine: Twelve of the 14 subjects who received 15 mg. of morphine found their reactions pleasant. Eleven of these called it the most pleasant of all the drugs in the series, and the 12th thought it equally as pleasant as heroin. One subject (Au.) had no reaction at all, and another (Hu.) reported "a slight sickish gurgling in my stomach, then a light sensation in my head." He was also somewhat sedated, said it was unlike anything he had ever had before, and called the experience the most unpleasant of the series. The pleasant reactions follow:

(Bar.): Shortly after the injection I felt a slight sensation in the pit of my stomach. At first I felt like I was going to get a glow as from a shot of heroin, but this subsided. Felt like a very weak shot of heroin or Dilaudid—the equivalent of ⅛ grain [8 mg.] of morphine or less. My voice got a little hoarse. About five or six hours after the shot I became very drowsy. Had no appetite at lunch and less than usual at dinner. I was very restless and wakeful until 2 a. m. The first few hours after getting the drug I was peppy and exhilarated. Had some drive, akin to Benzedrine. None of my usual muscular and bone aches yesterday. Severe headache in afternoon and evening. Think I had a narcotic of some sort.

(Warr.): A very good feeling. Like ⅜ grain [25 mg.] of morphine. Would like more of this. Good appetite. Slept unusually well.

(Gos.): Slightly "high." Little nervous. Can't say what it was.

(War.): Feels like ½ grain of morphine or an equivalent amount of heroin. No unusual physical sensations. Dose not big enough. About 10 hours after the injection I was extremely nervous and shaky for 30 to 45 minutes.

(We.): Feel better than normal. An increased dose might produce a euphoria. Think I had a little Demerol.

(Si.): Believe it was a very small dose of morphine. Not enough to actually feel but just enough to change.

(Ol.): Probably morphine, either a small dose or mixed with something else. Between 15 and 20 mg. Groggier than yesterday [heroin].

(Cl.): Reminds me of morphine. About ¼ grain. Relaxed, talkative, hungry, dry throat. This medicine seems to relieve me of my present worries and puts me in a peaceful state of mind. Contented. Felt that way for 10 hours. Slept better than in months.

(Sh.): A feeling in the pit of the stomach like when I shoot heroin. Kind of a lift. More like small dose of heroin than anything I know. More alert. Can think quickly. Puts me in a relaxed state of mind. Energetic. Better sleep than usual at night.

(Sm.): I got quite a growling feeling in the pit of the abdomen. Reaction is like ⅛ grain of morphine. Stayed with me for about 12 hours. Slept little sounder than usual. Nervous tensions. Tingling. Nice mood . . . talkative. Could be 5 mg. of heroin. More alert.

(Do.): A slight tickling in different parts of my body. My moods were altered a little—calm, amused, talkative. Ate four times as much lunch as usual. Slept real well at night.

(Gl.): A slight cocaine reaction—pleasant, peaceful and calm. Dream-like. Very good. Slept nice at night. Nice appetite.

Sixteen subjects were given 22.5 mg. of morphine. Eight of these called this experience pleasant (five of them considering it the most pleasant drug), and three considered the experience unpleasant. Of the latter three, one considered the drug tied with heroin for worst drug, and another considered it least objectionable of the drugs but unpleasant. Two subjects described no reactions at all. Three others considered their reactions neither pleasant nor unpleasant. Their reactions follow:

(Wal.): I was sleepy and tired when I arrived. After taking today's medication I no longer felt tired or sleepy. I also experienced a slight itch.

(Jo., J. W.): Felt slight effect but don't recognize the drug. Not enough to notice any change.

(Jo., B.): No sensation—not even a buzz. But later at night I was restless about going to sleep. This is very unusual for me.

The pleasant reactions were as follows:

(Gon.): At first I felt pretty good. Mouth sort of dry. I had a funny taste like Dolophine, but I think the kicks were something like Demerol. Later I went to sleep until supper time [very unusual]. Smoked quite a bit. Had no appetite at supper or the next morning.

(De.): Started feeling slowly a relaxed feeling that reached its peak in 30 minutes. Still felt satisfied and content two hours later. Feel as though I could go to bed and read and go to sleep. Noticed a peculiar drug taste in mouth. I would guess it was 100 mg. of Demerol. I would not want any bigger dose. I am satisfied the way I am now. Was comfortable the rest of the night. Very relaxed and contented. Good night's sleep.

(Cr.): Definitely had something—between Benzedrine and a narcotic. Can't name it.

(Pe.): Felt like ⅜ grain of morphine.

(Ni.): Relaxed, confident, and at ease. Like 15 or 20 mg. of Dolophine. That's the real stuff. I would very much like to repeat. Stayed nice all night. Woke up feeling normal.

(Da.): This helped me. It was Dolophine.

(Br.): Like morphine—in the stomach, and tightness in neck. Relaxed, calm, and peaceful. But only a slight reaction. Slept well.

(Fo.): A slight buzz. Butterflies in stomach. No reaction like this before. Restless later but slept O. K. at night.

The unpleasant reactions were as follows:

(St.): Slight suspicion of nausea in lower abdomen. Flushing and feeling of slight stimulation but not a true narcotic feeling—more like a synthetic but mixed with something that later causes nervousness and nausea. Didn't sleep at all at night. Too much stimulation.

(Gr.): No reaction except nausea and vomiting after dinner [5 to 6 hours after injection].

(Ba.): Sleepy and nervous. Nausea. No appetite. Little groggy. Slept all right. Reminds me of LSD [*d*-lysergic acid diethylamide].

Comparison of Drugs on Basis of Questionnaire: As in the case of the normal subjects, a comparison of the drugs was also made on the basis of responses to the questionnaire. The items were essentially those used in the normal group, with 21 items in the mood group, 5 items in the state-of-wakefulness group, and 6 items dealing with mentation. The results are shown in tables 7, 8 and 9. The results of the questionnaire generally corroborate the subjective descriptions of the postaddicts ex-

cept for the failure of the questionnaire to account for the reactions experienced after the initial two hour period had elapsed. Thus it will be seen that amphetamine was quite successful in improving mood in the group and indeed compared favorably in this regard with the opiates. The poor showing of the drug in the final estimates by the subjects seems due to delayed effects during the remainder of the day (anorexia, jitteriness, restlessness) and night (insomnia). This is substantiated by the responses to the item "would very much like to repeat this medication . . . wouldn't like to go through this again." These responses are tabulated in table 10, and indicate that, during the two hour period encompassed by the questionnaire, amphetamine was considered pleasant by half of the postaddicts.

TABLE 7.—*Questionnaire Scores on Mood Items in Thirty Postaddicts*

	Euphoric		Dysphoric		Group Mean Score	
	No.	Mean Score	No.	Mean Score	Euphoria	Dysphoria
Placebo	5	17	6	12	1	..
Amphetamine	20	32	5	14	19	..
Heroin	15	35	4	13	16	..
Morphine	22	38	3	4	27	..

TABLE 8.—*Questionnaire Scores on Sedation Items in Thirty Postaddicts*

	Sedated		Stimulated		Group Mean Score	
	No.	Mean Score	No.	Mean Score	Sedated	Stimulated
Placebo	4	4	4	3	..	..
Amphetamine	4	6	19	9	..	5
Heroin	9	6	7	4	1	..
Morphine	13	10	5	4	4	..

TABLE 9.—*Questionnaire Scores on Mentation Items in Thirty Postaddicts*

	Impaired		Improved		Group Mean Score	
	No.	Mean Score	No.	Mean Score	Impaired	Improved
Placebo	2	8	3	12	..	1
Amphetamine	3	8	16	11	..	5
Heroin	3	8	9	14	..	3
Morphine	2	8	16	13	..	6

In contradistinction to the college students, the postaddicts more frequently reported stimulation and improved mentation after the opiates. Particularly striking are the differences in mentation scores. Whereas the student volunteers almost invariably felt a dulling of senses after morphine and heroin, only 5 of the 60 postaddict questionnaires filled out after these opiates indicated impairment of mentation.

COMMENT

There is considerable variability in the meaning assigned to the word euphoria by different investigators. We have considered it as synonymous with a pleasant state as defined by our subjects. Since the issue was the production of euphoria by a given medicament, the subject's decision involved a comparison with the predrug state. Euphoria was, therefore, considered to have been produced when a feeling state resulted that was more pleasant than that obtaining before the injection of the drug.

We have attempted to avoid some of the more obvious pitfalls in this field. There has, for example, been a strong tendency for textbook writers to describe the central nervous system effects of a drug like morphine in oversimplified terms and sweeping generalizations, as if morphine produced certain set effects that were evident in all persons at all times, or at least most persons at most times. It is obvious that the subjective effects of drugs, no less than the objective effects, are dependent on the situation in which the drug is administered. It is also likely that the production of a given mental state, even in the same situation, will not prove equally pleasant to all persons. In addition, of course, there are such problems as the effects of dosage, route of administration, and duration of treatment. All of these considerations emphasize the need for carefully defining the conditions of the experiment in question.

Our results indicate, however, that in a defined experimental situation meaningful data can be obtained in the investigation of mood effects of drugs. For example, the precautions of random presentation and double-blind controls render it difficult to ascribe to chance and suggestion a similarity in the response patterns described by a majority of subjects for any one drug. Thus the ability of most of our normal subjects to pick out the placebo by their lack of response, the generally unpleasant state observed after the larger doses of morphine or heroin, and the generally pleasant effects of amphetamine are strong evidence that the elicited responses are reliable. There is further corroboration in the consistency of response on repeat experiments.

TABLE 10.—*Postaddict Responses to Questionnaire Item on Repeating Drug Experience*

	Would Like to Repeat	Would Not Like to Repeat	No Feelings One Way or the Other
Placebo	1	4	25
Amphetamine	16	3	11
Heroin	14	3	13
Morphine	17	2	11

We have been impressed by the usefulness of the questionnaire (or check list) approach in much of the work in our laboratory on subjective responses. Such questionnaires are primarily of importance in helping subjects to verbalize their responses. For many subjects, this is unnecessary, but for others the communication of subjective effects is difficult. It has seemed valuable to present such persons with opposing words or phrases, so that, although no one word or reaction is suggested in a biased fashion, such words as seem appropriate to them can be used in their descriptions. Certain semantic problems arise in the use of such aids. Often, a subject will find a given word close to the right feeling but not exactly right or will visualize a different meaning for a given word than the examiners (or most persons) have in mind. For these reasons, we think it important to go over the responses with the subjects at the end of the experimental period. Such a procedure also helps to elucidate what we have termed secondary psychological interpretations of drug effects, such as dysphoria because of sedation "when I didn't want to feel sleepy" or because of fear of "losing

control." Dissection of such complex responses, which are no less real than the uncomplicated primary sedation, yields more information, in our opinion, than the mere recording of such effects of a drug as "an unpleasantly sleepy state."

Normal Subjects.—The results described in the normal volunteers are in keeping with the data obtained in a previous pilot study on nine subjects. In both sets of experiments, amphetamine, in a dose of 20 mg., was a more potent euphoriant than morphine (in 8 or 15 mg. doses) or heroin (in 2 or 4 mg. doses). The experiments exploring the possibility that the doses of narcotics used were too large for optimal euphoria provided little support for such a thesis. Thus 1 mg. of heroin or 4 mg. of morphine produced little response of any sort in our subjects. It was decided not to explore higher doses in the normal volunteers, because we had used the usual clinical doses and because of the possibility of producing side-effects even more unpleasant and longer-lasting than those observed in the course of the standard experiments.

Our data thus indicate that morphine and heroin, in the described situation and doses, were not pleasant drugs to the majority of subjects. We cannot confirm the frequently quoted statement that nausea and vomiting after morphine "is not associated with the usual unpleasant emotional reactions." [1] A number of other observers have also expressed disagreement with the oft-described universal euphoriant effects of opiates.[2] Kolb [3] has said that "only in rare instances, if at all, does any one except the emotionally unstable, the psychopath, or the neurotic" experience positive pleasure from morphine. Fraser and Isbell [4] as well as Brown [5] have described the reaction to morphine of the person who is not an addict as one of indifference or actual dislike. Reichard [6] reports that dysphoria frequently results when a normal person is given an injection of morphine, and he describes morphine effects as "not a universally pleasant experience." Kuhn and Bromiley,[7] studying the effects of morphine on pain threshold, were surprised at the lack of euphoria in any of their volunteer subjects. Starr [8] has said that, in years of blindfold experiments with students at the University of Pennsylvania Medical School, the subjects have almost invariably found it difficult to understand why anyone should ever become addicted to morphine. Prescott and co-workers [9] observed no euphoria after morphine in eight medical student volunteers.

Such findings are in keeping with usual clinical experience, although not in accord with the statements in nearly all textbooks of pharmacology. The use of morphine for relief of pain is rarely followed by a true euphoria. Out of 386 doses of morphine (10 mg.) administered to 150 patients after operation in recent analgesic studies in this laboratory, on only 14 occasions did the patients (either by statements on questioning or by their appearance) suggest any reaction that might conceivably be called euphoric. In 11 of these instances, the responses consisted of phrases like "feel much, much better," suggesting merely gratitude for relief of pain. In only three patients were the responses really euphoric (e. g., "I feel in the clouds." "This medication makes me really feel wonderful.") Lee [10] has had similar experience: "Opiates used in their minimal effective clinical analgesic dose do not produce mental pleasure in most individuals." Further corroboration can be found in the reactions of our chronically ill patients described above under Results, and in the admittedly low incidence of morphine addiction resulting from the widespread legitimate use of morphine for pain relief.

Of interest to us was the similarity between morphine and heroin in our data, beyond the difference in actual weight of drug required to produce a given effect. The results with heroin did not justify its reputation as a great stimulant or as a producer of intense euphoria. In the frequently quoted study of Seevers and Pfeiffer,[11] in which heroin is said to have produced more euphoria than morphine, euphoria is defined as "the opposite of narcosis or . . . stupefaction. The absence of side actions after heroin . . . may account in some measure for the pleasurable reaction to the drug." In another section of this same paper, the authors state, "Not the slightest evidence of desire for repetition . . . by any of the individuals . . . a hearty dislike for the procedure was generally expressed." An examination of the literature reveals little or no critical evidence that this drug, when used for the same purposes for which morphine is used, and in equieffective doses, would be more apt to produce medical addicts than morphine. Perhaps a reevaluation of this drug's place in medicine is in order, particularly in view of claims made as to its superiority as an antitussive [12] and analgesic.[13] Studies in this laboratory in a group of patients with chronic cough suggest that heroin may perhaps excel codeine in suppressing clinical cough. More controlled work is needed before a sound appraisal of heroin's advantages and disadvantages is possible.

1. Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics: A Textbook of Pharmacology, Toxicology, and Therapeutics for Physicians and Medical Students, New York, the Macmillan Company, 1941.

2. Krueger, H.; Eddy, N. B., and Sumwalt, M.: The Pharmacology of the Opium Alkaloids, Pub. Health Rep., Supp. 165, 1941.

3. Kolb, L.: Pleasure and Deterioration from Narcotic Addiction, Ment. Hyg. **9**: 699-724 (Oct.) 1925.

4. Fraser, H. F., and Isbell, H.: Comparative Effects of 20 Mgm. of Morphine Sulfate on Non-Addicts and Former Morphine Addicts, J. Pharmacol. & Exper. Therap. **105**: 498-502 (Aug.) 1952.

5. Brown, R. R.: Order of Certain Psycho-Physiological Events Following Intravenous Injections of Morphine, J. Gen. Psychol. **22**: 321-340 (April) 1940.

6. Reichard, J. D.: Can the Euphoric, Analgetic, and Physical Dependence Effects of Drugs Be Separated? I. With Reference to Euphoria, Fed. Proc. **2**: 188-191 (Sept.) 1943.

7. Kuhn, R. A., and Bromiley, R. B.: Human Pain Thresholds Determined by the Radiant Heat Technique and the Effect upon Them of Acetylsalicylic Acid, Morphine Sulfate and Sodium Phenobarbital, J. Pharmacol. & Exper. Therap. **101**: 47-55 (Jan.) 1951.

8. Starr, I.: Personal communication to the authors.

9. Prescott, F.; Ransom, S. G.; Thorp, R. H., and Wilson, A.: Effect of Analgesics on Respiratory Response to Carbon Dioxide in Man, Lancet **1**: 340-344 (Feb. 26) 1949.

10. Lee, L. E., Jr.: Can the Euphoric, Analgetic, and Physical Dependence Effects of Drugs Be Separated? II. With Relation to Analgesia and Clinical Experience, Fed. Proc. **2**: 191-201 (Sept.) 1943.

11. Seevers, M. H., and Pfeiffer, C. C.: A Study of the Analgesia, Subjective Depression, and Euphoria Produced by Morphine, Heroine, Dilaudid and Codeine in the Normal Human Subject, J. Pharmacol. & Exper. Therap. **56**: 166-187 (Feb.) 1936.

12. Pottenger, F. M.: Tuberculosis: A Discussion of Phthisiogenesis, Immunology, Pathologic Physiology, Diagnosis and Treatment, St. Louis, C. V. Mosby Company, 1948. Fishberg, M.: Pulmonary Tuberculosis, ed. 4, Philadelphia, Lea & Febiger, 1932.

13. Lund, C. J., and Harris, J. W.: The Use of Heroin (Diacetyl-Morphine) in Labor: A Report of 454 Deliveries, Am. J. Obst. & Gynec. **45**: 980-991 (June) 1943.

Although amphetamine is generally acknowledged to be capable of inducing euphoria,[14] we were surprised at the intensity of this response to the drug. The descriptions of our normal subjects after receiving amphetamine were closer to the usual textbook and literary descriptions of the euphoric effects of opiates than were the reactions to morphine and heroin. The reasonably large dose of amphetamine and the parenteral route used presumably aided in the production of striking euphoria. This drug is frequently used illicitly, and true addiction may occur, according to Knapp.[15] The eagerness of our subjects to repeat their experience with this drug (see table 5) emphasizes its possible dangers in this regard. The chronically hospitalized patients showed a similar tendency to prefer amphetamine over opiates. This latter group of subjects would probably have shown a more striking difference between the effects of amphetamine and the opiates if larger doses (such as those used in the normal subjects) had been used. There is, it appears, a real place for amphetamine as a euphoriant in the treatment of the hopelessly ill.

A further point of interest is the apparent pain relief after amphetamine in the chronically ill group. Although it is sometimes suggested that the ability to produce euphoria is an intrinsic part of the analgesic effect of morphine, it would seem that in most instances analgesia can be obtained without a positive euphoria.[10] In view of the claims in the literature that amphetamine is an analgesic agent,[16] the question arises as to what role euphoria plays in the analgesic effects that some have claimed for this drug. In an investigation in this laboratory of the pain-relieving power of amphetamine in patients with severe postoperative pain, we have not been impressed with either the euphoria or analgesia following 10 or 20 mg. of amphetamine given subcutaneously. Such results emphasize again the need for operational concepts in discussing the effects of drugs.

The importance of placebo controls is demonstrated by tables 2 to 5. For example, the mean euphoric scores for placebo, heroin, morphine, and pentobarbital are essentially the same. Likewise, the mean scores for sedation and impaired mentation after placebo and amphetamine are almost identical. Finally, the incidence of "would like to repeat" responses was essentially the same for placebo, morphine, heroin, and pentobarbital. Obviously a yardstick is essential for measurements, and the absence of placebo data to serve as such a yardstick would lead to unjustified conclusions in the above instances.

Although such objective behavior as occurred during the testing usually paralleled subjective descriptions, in general the outward manifestations of the drugs used contributed little to a recording of experienced effects. The use of group studies and social situations, with greater opportunity for interpersonal responses, would perhaps have been more productive in this regard, and are planned.

Postaddict Group.—The results in the postaddict population were of considerable interest. This group was included in the study for several reasons: 1. Addicts represent a population subgroup that is of fundamental interest for the entire addiction problem. 2. The postaddicts, although healthy male volunteers, differed from our normal volunteer group in age, in the inclusion of Negro males, and in social background, educational background, and drug experience. 3. The experimental situation (i. e., a narcotics prison) was considerably different from the environment in which our normal volunteers were studied.

In some respects, however, the results in these two groups were alike. For example, both postaddicts and normal volunteers picked out the placebo most frequently as having produced no reaction at all. In addition, amphetamine, as in the case of the normal subjects, was quite successful in creating a pleasant state in many of the postaddicts. A third point of similarity was the absence of marked euphoria after heroin; with the route and doses used, this drug was actually inferior to morphine in producing a feeling state that was desirable to the postaddicts. There were important differences, however, between the normal volunteers and the postaddicts. The latter group, for example, most frequently picked morphine as the most pleasant drug of the series, whereas the normal subjects most frequently picked it as most unpleasant. The situation with regard to amphetamine was just the reverse, i. e., it was most frequently chosen by the postaddicts as most unpleasant, whereas this drug was the most pleasant drug for the majority of normal volunteers. The postaddicts differed markedly from the normal volunteers in other reactions to opiates, i. e., in the reported infrequency of mental dulling, nausea, vomiting and other side-effects.

Variables: The postaddicts differed from our other volunteers in so many respects that one can only enumerate a number of variables that might conceivably be of importance in explaining differences in the data. We cannot escape the fact that in the case of the addicts the experimental environment was that of a prison, with all the restrictions and connotations implied. In view of the previously described administration of narcotics to all of the addict subjects within a matter of days prior to the onset of these experiments, the difficult problem of residual tolerance to narcotics in these subjects also deserves mention. The histories of the addict volunteers indicated that almost without exception they had become sick on first exposure to narcotics (even in relatively small doses) but that they claimed the development of tolerance to the emetic effects with subsequent doses. The low incidence of nausea and vomiting with the doses used in the present experiments suggests a certain degree of tolerance in the postaddicts, since these doses were similar to those that had caused gastrointestinal symptoms on first exposure on the outside and were in the range extremely likely to cause nausea or vomiting in the normal subjects. On the other hand, prolonged effects

14. Davidoff, E., and Reifenstein, E. C., Jr.: The Stimulating Action of Benzedrine Sulfate: A Comparative Study of the Responses of Normal Persons and of Depressed Patients, J. A. M. A. **108**: 1770-1776 (May 22) 1937. Gwynn, H. B., and Yater, W. M.: A Study of the Temporary Use of Therapeutic Doses of Benzedrine Sulfate in 147 Supposedly Normal Young Men (Medical Students), M. Ann. District of Columbia **6**: 356-359 (Dec.) 1937. Nathanson, M. H.: The Central Action of Beta-Aminopropylbenzene (Benzedrine): Clinical Observations, J. A. M. A. **108**: 528-531 (Feb. 13) 1937.

15. Knapp, P. H.: Amphetamine and Addiction, J. Nerv. & Ment. Dis. **115**: 406-432 (May) 1952.

16. Goetzl, F. R.; Burrill, D. J., and Ivy, A. C.: Analgesic Effect of Dextro-Amphetamine Alone and in Combination with Morphine Sulphate, Fed. Proc. **2**: 16 (March) 1943. Nickerson, M., and Goodman, L. S.: Synergistic Isonipecaine-Amphetamine Analgesia, ibid. **6**: 360-361 (March) 1947.

from amphetamine seemed actually more frequent in the addicts than in the students. It would be of interest to repeat the experiments in such a group of postaddicts when all narcotics had been withheld for six months or so. Also of interest would be a study in postaddicts with less experience with drugs than the present group. Andrews,[17] and Fraser and Isbell,[4] have presented data to support the theory that postaddicts are less susceptible to certain narcotic effects even after prolonged abstinence from opiates.

The effect of increasing the dose of each drug one and one-half times cannot be stated with any precision, since the two dosage groups in the experiments with postaddicts were composed of different persons. Nevertheless, certain trends were evident. In the case of morphine, there was no particular evidence of a dose effect. In the case of heroin, there was a suggestion that more persons considered the larger dose unpleasant, and fewer of the white prisoners considered their reactions to this dose as neutral. With amphetamine, the larger dose seemed to cause unpleasant reactions more frequently in the white prisoners, and there was a suggestion that more of the Negro addicts found the larger dose pleasant.

An important consideration in the experiments with postaddicts is the tremendous past experience of these subjects with a variety of drugs. It was expected that such subjects would be less likely to be fooled by placebos and better able to identify narcotics. In general, the latter statement was true. It is of interest, however, how many errors were made. For example, the placebo reaction rate was about the same as in the college students. An examination of the guesses on the drugs chosen as most pleasant (the case in which guesses were most frequently correct) shows that heroin and morphine were correctly identified only five times, although on five other occasions they were either confused with each other or called "heroin or morphine—I don't know which." Morphine was considered to be methadone twice, "Demerol" twice, "a narcotic" once, a "synthetic" once, and cocaine once. Heroin was called "Demerol" twice, "Dilaudid plus cocaine" once, "morphine plus cocaine" once. On two occasions, morphine was described as "nothing I ever received before." Amphetamine was called "cocaine" four times and not recognized twice by the six addicts who found the drug "most pleasant." In fairness, it should be pointed out that several factors were operating to the disadvantage of the addicts in guessing the nature and amount of narcotics given to them. First, most of these men usually receive their narcotics by the intravenous route; a few had never taken drugs subcutaneously. Second, the doses of narcotics may have been too small (at least for some) and thus not optimal for identification purposes. Third, a few addicts had had experience primarily with one narcotic, e. g., morphine, and almost none with heroin, or vice versa.

Within the addict population, it seemed pertinent to investigate the possible effect of such factors as age, race, and intelligence quotient on drug responses. Such a dissection is, however, impossible because of the numerous variables clustered together in the groups. For example, the Negro addicts were not only younger but also had lower intelligence quotients, fewer years of narcotic experience, and were more likely to have had non-narcotic criminal records. In addition, the white addicts were typically addicted to morphine or dihydromorphinone, whereas the Negro addicts preferred heroin, cocaine, or marihuana, if given a choice of drugs. Differences between white and Negro addicts should therefore be interpreted as merely descriptive of the results in two groups, without regard to the relative importance of any one factor (e. g., race) in determining responses. With these limitations, it may be said that the Negro addicts seemed to have a greater incidence of pleasant reactions from amphetamine, the whites a higher number of unpleasant ones. The larger dose of heroin, and both doses of morphine, seemed to yield more pleasant reactions and fewer neutral responses in the white than in the Negro subjects.

Another possible orientation of the data is in relation to the drug preferred by the addict in a nonprison environment. Of the 10 addicts who preferred morphine or dihydromorphinone on the outside, all but one picked morphine during the test series as the most pleasant drug. The addicts, of course, were not made aware of the nature of the drugs until after all data were collected. Of the 13 who stated a preference for heroin in civil life, 8 picked morphine as the most pleasant drug, 4 picked amphetamine, and only one picked heroin. Of the four addicts who liked cocaine best on the outside, two picked amphetamine as the most pleasant drug of the experimental series, one picked heroin, and the fourth considered heroin and morphine equally pleasant. There were two who smoked opium by preference on the outside; one preferred heroin and one morphine during the experiments. The single addict who preferred marihuana had no reaction from any of the four drugs in the series.

Difficulties in Use of Postaddicts: All of the above considerations point out certain real difficulties in the use of postaddicts. Many of these persons are pharmacological sophisticates, i. e., they can not only accurately distinguish between a potent drug and a placebo but can identify certain drugs with amazing accuracy, regardless of route of administration. In such persons, when the drug in question is one strongly laden with meaning and importance for them, the results in a given experiment may be colored by a long-standing and complex drug-person relationship that does not exist in nonaddicts. A further confusing point is that, while one would be foolish to deny the importance of opiates for addicts, it is difficult to be sure of the source and the nature of the satisfaction derived. Thus some of the addict volunteers questioned found the physical "sensation" of opiates most pleasing, others the "energy and drive," others the "relaxed feeling," and still others the "happy, sociable" state realized only with drugs. Besides these differences in the descriptions of pleasurable feeling states, there were varying preferences for drugs on the outside. In many instances, this preference seemed predetermined by the drug to which the addict was first exposed or to which he first became addicted. In other cases, there was an expressed preference for one drug over another because of such factors as differences in speed of action (some preferring a rapid change, others not), duration of action (most preferring a long-acting drug), and degrading

17. Andrews, H. L.: The Effect of Opiates on the Pain Threshold in Post-Addicts, J. Clin. Invest. 22: 511-516 (July) 1943.

nature of one drug as compared with another (certain addicts believed some narcotics to produce more vicious habits or to have more deleterious effects on social behavior). Not in all instances did the addicts' statements agree with generally accepted pharmacological opinion as to drug actions (e. g., some addicts believe the effects of morphine to be of shorter duration than heroin). An important factor that may overlay many responses is the long-term conditioning that usually begins before the first experience with narcotics, i. e., the almost universal anticipation by addicts (based on conversation with, or observations of, other addicts) that opiates will produce a pleasant state of some sort. How to dissect out this factor of suggestion from subsequent drug reactions in such persons poses a problem almost impossible of solution.

In addition, it must be remembered that all of the addicts studied were volunteers and differed in this and other respects from other inmates at the institution (see description under Methods). The possibility must be entertained that data derived on such "chronic" volunteers, with long histories of illicit drug use, may not be transferable to other addicts in the same institution, let alone to addicts at large in the general population. In this regard, something should be said about the so-called normal volunteers used in our experiments. Although none of our normal subjects had had previous narcotic experience, some of them participated not solely to earn money but primarily for the new experience (by their own admission). In our culture, the stigma attached to drugs is such that a person volunteering as a subject for experimentation with such agents is flouting traditions, and sometimes family opinion, in order to do so. In these respects, such volunteers resemble potential addicts.

A final point concerns the question of predicting addiction liability of old and new drugs. Ethical considerations dictate the use of postaddicts in assessing the development of tolerance and physical dependence. It is hard to envision such studies in other volunteer groups. On the other hand, the labeling of a drug as pleasant or unpleasant on the basis of expressed preferences of a group of addicts may be misleading in the prediction of euphoriant capacity of a drug in patients. This may lead to dismissing one drug or underestimating the potential uses and hazards of another drug. It is fairly obvious that the incidence of addiction to a drug in an addict population is a composite of availability, price, purity, suggestion, legal codes, cultural attitudes, psychological needs, and socioeconomic pressures, to name some of the more obvious factors. In view of this fact, and the acknowledged discrepancy between the nature of addiction produced by legitimate prescription of drugs and that obtaining in the majority of addicts, it would seem wise to distinguish carefully between law enforcement problems —important as they may be—in illicit narcotic traffic, and medicolegal restraints and safeguards in the legitimate use of drugs. Much of the thinking and writing on addiction seems to confuse these two reasonably distinct areas by formulating simple generalizations and legal codes to cover all contingencies. The tremendously complex field of drug addiction deserves a more sophisticated and scientific approach.

SUMMARY

Normal subjects; chronically ill, hospitalized patients; and postaddicts were studied to determine their subjective responses to a series of drugs. In the normal subjects, and to a lesser degree in the chronically ill patients, amphetamine surpassed morphine, heroin, pentobarbital, and a placebo in its ability to produce a pleasurable state. The drug most frequently associated with a dysphoric state was morphine. The majority of postaddicts considered the effects of morphine more pleasant than those of heroin, amphetamine, or the placebo. Amphetamine was the drug most often described by them as unpleasant. The latter judgment seemed due in large part to unpleasant and prolonged side-effects of amphetamine, such as insomnia and anorexia. In addition to dose and route of administration, the nature of the subject and the situation in which a drug is administered are important determinants of drug effects. This operational concept deserves greater emphasis in current pharmacological texts and teaching.

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The Board of Trustees of the American Medical Association, with the approval of the House of Delegates, appointed a committee that has been called the Committee on Relationships Between Medicine and Allied Health Agencies. Several articles will appear under the auspices of the committee explaining the origin, organization, and work of some of the well-known agencies. Following is the third of the series.—ED.

THE PHYSICIAN AND THE VOLUNTARY HEALTH AGENCY

THE AMERICAN HEART ASSOCIATION

John W. Ferree, M.D., New York

The rapid growth of the American Heart Association and the vigorous development of its program since its reorganization six years ago have demonstrated the important role of the physician within the framework of a voluntary agency in helping to meet one of the nation's primary health problems. As the Heart Association pursues its objectives, the ideal of partnership between the medical profession and the lay public emerges as the key factor in assuring the success of its program. On the national, state, and particularly on the community level, the physician has been accorded new opportunities to raise his stature in the eyes of the public and make more effective the services he performs to reduce death and disability from the cardiovascular diseases. Occupying as he does a respected and authoritative position in the community, the physician has found that he can extend his role of counselor and guide through his participation in the local affiliated heart association. This has meant a broadening of the physician-patient relationship and the involvement of a community service team, with the physician as its leader.

So firm is the recognition of the need for physician leadership and cooperation that the assembly of the American Heart Association, the over-all governing body

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Director, Community Service and Education, American Heart Association.

composed of both physicians and laymen, approved the following recommendation at its annual meeting in Chicago last April: "That all Heart Associations establish close liaison with the constituent societies of the AMA for the purpose of encouraging physician participation in the local heart program. It is suggested that Heart Associations work closely with the Medical Societies' committees concerned with public relations and ethical standards, and that physicians as well as laymen be included in the membership of the Heart Associations' public education committees." The assembly also recognized "the importance of patient education by the physician" and recommended "the preparation by the AHA of educational materials which will assist the physician in advising the patient how to live intelligently with his heart condition." A number of such pamphlets are already in print, and they are helping physicians to clear away patients' misconceptions and fears.

These recommendations reflect an increased awareness of the role the physician can play not only in the physical health of the patient but in his mental attitudes as well. In fact, the change in the general public attitude toward diseases of the heart and blood vessels, with the supplanting of fear and fatalism by a new determination to bring the cardiovascular diseases under control, has been one of the dramatic achievements. This has been brought about over the past few years largely through the public education program of the Heart Association. Restated in reference to the doctor's practice, such a changed attitude means a more understanding and cooperative patient. Today the American Heart Association can also report gratifying progress in other areas of its comprehensive program, in addition to public education. As mounting public support makes additional funds available, the financing of scientific research, the development of professional education programs, and the organization of community services conducted by its affiliates are beginning to assume the proportions required to meet the increasing problems of cardiovascular disease.

HISTORICAL BACKGROUND

The current growth of a dynamic program in the cardiovascular field represents a heart-warming reward for the efforts begun by the physician founders of the American Heart Association over three decades ago. The association was originally conceived primarily as a professional scientific body by a small group of physicians who recognized the grave threat of cardiovascular diseases to the nation's health. The forerunner and parent body of the American Heart Association, and also of the New York Heart Association, was the Association for the Prevention and Relief of Heart Disease. The parent association, constituting the first organized effort of its kind to collect and apply information on heart disease, was formed in May, 1916, as the result of a series of conferences among New York physicians, which were stimulated by cardiac rehabilitation work at Bellevue Hospital. Increasing interest in this work prompted the New York group to invite approximately 100 physicians from all parts of the United States to a meeting in St. Louis on May 24, 1922, to plan for a national organization. Two years later, on May 20, 1924, the American Heart Association was formally incorporated under the laws of New York State.

In the ensuing years, the association conducted a limited program of professional education; however, it became increasingly apparent that the complex problems of cardiovascular disease could not be solved by the medical profession alone. Organized voluntary action and the cooperation of the lay public were needed to provide and to coordinate the many, varied, and costly resources required for an attack on the cardiovascular problem. The innumerable social, economic, and personal complications created by heart disease required an approach of much greater scope and magnitude than anything that had previously been attempted. Above all, the program required much greater support for cardiovascular research to uncover new knowledge, the channelling of new and existing information to the public as well as to physicians and allied professional groups, and the development of community services for the patient with heart disease. The organization of local affiliated associations also was necessary to provide the community facilities and resources to supplement the efforts of physicians in applying knowledge for the better management of patients with heart disease.

The concept of the service team, functioning as part of the organized community, with the physician spearheading efforts to integrate the threefold program of research, education, and community service, was to be blueprinted and put into action when the association was converted into a voluntary health agency in 1948. This step resulted in the admission of laymen to membership and to places on the association's governing bodies for the first time. The accelerated progress of the association since then is evidence both of the public's confidence in and acceptance of its program and of the physician's willingness to assume a position of leadership and responsibility. At present the association and its affiliates have a voting membership of about 25,000, almost evenly divided between physicians and laymen. There are now 56 state and regional affiliates and more than 350 local chapters. The national headquarters in New York administers the national phases of the heart program, provides educational and program guidance materials and services, and maintains a clearinghouse of ideas and suggestions for the work of state and local associations and committees.

EIGHT MILLION DOLLARS SPENT TO AID RESEARCH

The program activities of the American Heart Association and its affiliates are financed primarily by public contributions during the annual February Heart Fund campaign. At least half of the funds received by the national office of the association are spent for research support, which has top priority in the heart program as the single most important factor by which it is hoped to achieve the ultimate conquest or control of the heart diseases. Most of the affiliated heart associations and their chapters make additional research awards in their own areas, over and above their participation in the national research support program. Since 1948, a total of approximately 8 million dollars has been allocated by

the association, its affiliates, and their chapters for research support. Such support is provided in the form of fellowships and grants-in-aid to investigators active in a wide variety of disciplines. Many of the research projects are basic studies. The association's Career Investigatorships, of which there are three at the present time, provide continuing support for qualified individuals throughout their productive careers. This principle of lifelong research support is unique among voluntary health agencies. Through its research committee, the association also coordinates its efforts with those of other agencies supporting research in the field.

The association's scientific program, including research and educational aids for the medical profession, is conducted by the scientific council, established at the time of reorganization to assure the maintenance of high scientific standards. This council includes five sections based on particular medical interests, namely, the sections on basic science, circulation, clinical cardiology, cardiovascular surgery, and the council for high blood pressure research. The council on rheumatic fever and congenital heart disease has independent status within the association. It includes representatives of 11 professional and voluntary organizations, in addition to the Heart Association, and serves to correlate activities in the field of its interest. The council on community service and education was recently organized to expedite the development of this phase of the Heart Association program. The council is concerned to a great extent with insuring that people in the community will benefit from latest research knowledge and that local facilities and services that will be of assistance to the physician are developed through affiliated heart associations. This council is also responsible for the development of the national lay informational and educational program.

The scientific council's professional education program, which seeks to make available to physicians the mass of new and existing knowledge, has its most notable expression in the annual scientific sessions. These sessions are regarded as the most comprehensive presentation of developments in the cardiovascular field. The 27th scientific sessions were held this year in conjunction with the second World Congress of Cardiology in Washington, D. C. Several of the council's sections hold additional scientific meetings, and affiliated heart associations schedule scientific meetings, forums, postgraduate courses, and other events for the medical profession in their areas, many of these in cooperation with the local medical societies. At annual meetings of the American Medical Association in the past few years, the American Heart Association has arranged series of question-and-answer panels on cardiovascular problems and has exhibited its professional materials, including Dr. J. Scott Butterworth's fluorodemonstrator, which won the Billings Gold medal at the 1952 A. M. A. Annual Meeting.

PUBLICATIONS FOR PHYSICIANS

The Heart Association's two scientific journals, the monthly, *Circulation*, and the bimonthly, *Circulation Research*, have become outstanding mediums for the publication of reports on clinical and basic science subjects. In addition, the bulletin, *Modern Concepts of Cardiovascular Disease*, reviews a specific cardiovascular subject each month. Handbooks, manuals, and other materials are also issued to help the physician in diagnosis, treatment, and prevention, and in keeping cardiac case histories. These include recommendations for blood pressure determination and for examination of the heart, a statement on antibiotic prophylaxis for streptococcic infections as a preventive measure against rheumatic fever, a book on nomenclature and criteria and a chart on functional and therapeutic classification of patients prepared by the New York Heart Association, standards for electrocardiography, recommendations on cardiac catheterization and angiocardiography, and minimum requirements for cardiac clinics. Standards for recording heart sounds and the production of tapes are being prepared. Heart models are distributed for medical teaching, and professional films and slides are made available through the association's film library. As a pioneering project to obtain information on teaching methods in less urban areas, the American Heart Association recently cooperated with the New Hampshire Heart Association and medical organizations within that state to conduct a series of postgraduate teaching programs.

Although recognizing the important role of the physician, and the need to provide him with the latest tools of knowledge, the Heart Association program, as has already been pointed out, also takes into account the many factors in the total management of the patients with heart disease that are beyond the limits of the practitioner's time and that lie in areas outside the scope of his training. Because cardiovascular disease is frequently long in duration and is accompanied by emotional and social problems of the patient and his family, the coordinated effort of the general physician, cardiologist, psychiatrist, pediatrician, and other specialists in allied professions, such as the nurse, social worker, nutritionist, occupational therapist, and rehabilitation worker, are essential.

COMMUNITY PROGRAMS—A RESOURCE FOR PHYSICIANS

Through the community service programs developed by affiliated heart associations under the guidance of the national office, invaluable assistance is rendered to the physician, enabling him to utilize effectively the varied community resources at his disposal. The affiliated heart association acts as a coordinating body, working with other community groups to integrate existing private and public facilities to avoid overlapping and duplication and to strengthen existing services and initiate plans for required new services. A typical community service program includes projects such as diagnostic clinics for patients with cardiovascular disease, rheumatic fever prophylaxis, rehabilitation services and work evaluation units, work simplification for the housewife with cardiovascular disease, vocational counseling, nutritional guidance for patients with heart disease, and home care.

The clinic has long been an important concern of heart associations and frequently serves as a focal point for expanding the entire community program. While heart associations do not actually operate the clinics, they help insure the best possible quality of services for the patient

by granting certification to local clinics that meet the standards established by the association's national committee on cardiovascular clinics. In addition to providing facilities for diagnosis and treatment, the clinic makes available facilities for medical research and professional education.

The association's rehabilitation program helps patients with cardiovascular disease remain independent, self-supporting members of society, thus bringing them psychological as well as economic benefits. A pioneering development in this area is the work classification unit, often attached to a cardiac clinic. The unit provides a counseling service to which physicians may refer patients with heart disease for assessment of their work capacity as a basis for selective placement in a job where they can perform fully without overtaxing their physical reserve. Together with other services, such as the sheltered workshop and vocational guidance, these units do much to aid the physician in the practical management of the patient at the same time that they cope with the problem of breaking down the barriers that still keep many capable patients with heart disease from productive employment. Rehabilitation principles have been adapted to the needs of the housewife with cardiovascular disease in the form of the Heart of the Home program, designed to teach housewives how to simplify their work habits and conserve their strength. Special courses and "heart kitchen" demonstrations have proved immensely popular throughout the country. Valuable assistance is also provided to the patient in the home through home-care programs, which include occupational and recreational therapy, social service, home nursing, housekeeping services, and other aids developed in cooperation with various community organizations.

Community programs for the prevention, control, and treatment of rheumatic fever are being developed in an effort to lessen this major health problem, which particularly threatens the hearts of young persons. Rheumatic fever committees of heart associations endeavor to work closely with the physician to encourage the widest use of antibiotic preventive techniques presently available. They support community diagnostic services, cooperate with school health authorities to develop screening procedures, and in some cases sponsor traveling clinics for isolated rural areas.

The problems of overweight and diet have occupied the attention of many heart associations in their community activities, but it is recognized that much more must be learned about these subjects. Meanwhile, for the protection of patients with heart disease and others following sodium-restricted diets, the American Heart Association, in cooperation with the Council on Foods and Nutrition of the American Medical Association and the Food and Nutrition Board of the National Research Council, has developed recommendations for more precise labeling of the sodium content of special dietary food products. These recommendations were recently adopted as official regulations by the Food and Drug Administration.

The lay educational program of the association, conducted on the national and local levels, has been a major factor, as already noted, in creating a climate of optimism and confidence that grows out of a rational understanding of heart disease and the place of the medical profession in combating it. This program has made much progress in imbuing the public with an awareness of the need for prompt and regular medical attention, at the same time avoiding fear appeals. To help develop this increased public awareness and support of the heart program, the association and its affiliates issue or distribute pamphlets, books, films, exhibits, and other materials on various aspects of cardiovascular disease for patients, their families, teachers and other specially interested professional persons, and the general public. Through press information services, the association and its affiliates maintain a constant flow of accurate and constructive information to all mediums of communication. The association publishes a quarterly periodical, the *American Heart*, to provide the general reader with a continuing progress report on advances in the heart program. Inquiry services are maintained by heart associations to answer specific questions from individuals and professional persons in need of information and advice.

COOPERATION WITH OTHER GROUPS

To assure a coordinated approach to the many problems posed by cardiovascular disease at the national level as well as in the community, the American Heart Association welcomes the opportunity to work closely with other interested and related organizations (especially the American Medical Association) in the United States and abroad. It contributes to the support of the Inter-American Cardiological Society and International Cardiological Society and is represented at most international cardiovascular conferences. The association has established close liaison with official health agencies, including the Public Health Service, the Children's Bureau, the Extension Service, and the Office of Vocational Rehabilitation. To promote a better understanding of the pathological basis for clinical disorders, the association cooperates with the Registry of Cardiovascular Pathology of the Armed Forces Institute of Pathology in Washington, D. C., through a special committee, aiding in the collection, study, and preservation of pathological materials of cardiovascular interest. The association cooperates with the American Board of Internal Medicine, Subspecialty Board on Cardiovascular Disease, in the examination of candidates for certification as cardiologists and advises the American Medical Association in certifying hospitals for residency in this specialty.

The American Heart Association is essentially dedicated to the advance of scientific and medical knowledge, and it is dependent upon the support and guidance of the physicians of this country in the furthering of research, the dissemination of information, and the development of other aspects of its program. The door to active participation is open to all physicians through membership in the affiliated community heart association, by means of which they may play an effective part in building the kind of heart program that is needed locally. As a voting member of his association, the physician has a voice in the national program as well. The advice, counsel, and constructive leadership of the physician is earnestly sought as new and more effective ways are charted to defend the nation's heart.

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NUTRITION AND DISEASE

The special issue of *Postgraduate Medicine* for March, 1955, with Dr. Tom D. Spies as guest editor is a comprehensive report of current knowledge of nutrition in health and disease. It is a product of the cooperation of the department of nutrition and metabolism, Northwestern University Medical School, Chicago; the nutrition clinic, Hillman Hospital, Birmingham, Ala.; the Hospital General Calixto García, Havana, Cuba; and the Hospital Mimiya, Santurce, Puerto Rico. These groups have compiled a large series of cases illustrative of various phases of dietary deficiency. A study of the pictures alone will give the viewer an increased awareness of what can be done for patients with a great variety of signs and symptoms.

In many parts of the world large segments of the population subsist on grossly inadequate diets. A hungry man is primarily interested in satisfying his hunger. He knows nothing of the nutritive components of common foodstuffs and does not realize that one essential nutrient cannot replace another and that if a single nutrient is omitted the body cells that require it remain "passive spectators" and leave the table still hungry. Although the goal of nutritional research is optimal nutrition, there are still many gaps in our knowledge of what constitutes such a state. Meanwhile there is a steady accumulation of information of value in diagnosing states of faulty nutrition. Since there is no specific laboratory test for any of the deficiency syndromes, the diagnosis depends primarily on a careful history and physical examination, with laboratory tests playing a secondary role. The physician must know what symptoms and signs to look for and how to recognize them when they are present.

The skin lesions of dietary deficiency may appear in any part of the body but are usually bilaterally symmetrical, well demarcated, and associated with burning or itching. In the mouth the presence of even a mild glossitis may be indicative of pellagra, and in some atypical cases this may be the only physical manifestation of the disease. This and other deficiency diseases may occur in (1) persons who because of poverty or whim get a faulty diet, (2) patients with organic disease, and (3) chronic alcoholics. Pellagra developed in one patient who was kept too long on a very restricted diet because of chronic hypertension. When a patient in a low income group is found to have pellagra, other members of the same household should be studied for early signs of the disease, because the dietary habits of a household are likely to be pretty much the same. The polyneuritis observed in patients with pellagra is essentially the same as that of patients with beriberi. The manifestations of pellagra are varied. Some patients with a subclinical or mild form of the disease are given an erroneous diagnosis of hysteria, an anxiety state, or neurasthenia. It is important to recognize the underlying cause in these patients, because treatment by any psychotherapeutic technique will not help them and a proper dietary regimen with an appropriate supplement of vitamins will effect a prompt cure. As a result of the better understanding of nutritional deficiencies the ravages of pellagra are no longer seen in the United States, and according to Dr. Guillermo García Lopez and associates and Dr. Ramon Suarez and associates endemic sprue is rarely seen in either Cuba or Puerto Rico. The relation between vitamin B_{12} and macrocytic anemia has already been commented on in these columns.[1]

There is increasing evidence that dental caries is in part at least the result of a faulty diet. The disease can be controlled in susceptible persons by rigidly omitting fermentable carbohydrates from the diet and giving them nonadherent, rough, coarse foods that clean the teeth by friction. When such persons "break training" their salivary dental caries activity test again becomes positive before any visible signs of dental caries appear.

That studies of human nutrition will continue to bring to the clinician fundamental knowledge about the prevention and treatment of disease cannot be doubted. Greater efforts will be made to find ways of detecting subclinical nutritional deficiencies so that corrective steps may be taken before any disability occurs. Already, important information on a patient's vitamin C status can be obtained from the concentration of ascorbic acid in the plasma. Spies and his co-workers believe that diseases are chemical in origin and that they can be chemically prevented and corrected. They have gone a long way toward proving their contention.

1. Relationship Between Vitamin B_{12} and Macrocytic Anemia, editorial, J. A. M. A. **157**: 244 (Jan. 15) 1955.

DANGER OF DISCARDING SAMPLES

An investigation in a fairly large American city has revealed a source of medical trouble probably not generally realized by the medical profession. From time to time there are reports of children becoming ill because they swallow the drug samples mailed to their physician fathers. Too often these samples are left in desk drawers, on tables, and in wastepaper baskets easily accessible to the curious child. More recently there has come to light a practice by which drug samples are collected and sold. Such a practice obviously is an open invitation to the unscrupulous to switch labels, mix drugs, and carry out other practices that can be harmful.

Some months ago the Food and Drug Administration determined that a person was selling a drug without a prescription and on inquiry learned he was obtaining part of his drug supply from a charwoman employed in a building in which there are many offices for physicians. She, in turn, was obtaining her supply from wastebaskets into which physicians had discarded professional samples

mailed to them or left by representatives of drug houses. This finding resulted in an investigation of several medical offices to learn how drug samples were used or discarded. One group collected the samples for distribution overseas, but the others had no provision for the proper disposal or control of discarded drugs, which could lead to illness or death in those tempted to use the drugs personally and to illegal diversion of dangerous drugs by those sufficiently unscrupulous to circumvent usual commercial practices.

It is important for physicians, for their own protection, for the protection of their children, and for the protection of others to dispose of unwanted drugs in a way that will prevent their subsequent misuse. It is not difficult to develop a procedure by which this problem can be controlled, and the results will more than repay the slight inconvenience of assuring this control.

THE EDITOR'S CORRESPONDENCE

The mailbox for most editors looks like a grab bag in a windstorm. Filled with surprises and never lacking in interest, it provides a cross section of medical opinion, of likes and dislikes. Some is published in the correspondence section of THE JOURNAL; some is answered directly from the Editor's office or is referred to a more appropriate office for reply; and some is handled with asbestos gloves. We are joking about the latter, of course, but the mail is varied and never dull.

From time to time readers of THE JOURNAL become indignant when their letters of protest about some action are not published in THE JOURNAL. They accuse the Editor of being high-handed and arbitrary, of being biased, and of being out of touch with the facts of life. And they may honestly believe they have good reason for such accusations. Unfortunately, some may not realize that THE JOURNAL is the official journal of the American Medical Association. It is published under the auspices of the Board of Trustees. It is not the property of the Editor. Therefore it, like the Board of Trustees and the Editor, must serve the interests of the Association, of medicine as a whole and not of one man. There undoubtedly are times when the editorial staff errs in its decisions, but someone or some group must make a decision, right or wrong. Furthermore, all of the policies of the Association and the actions, past, pending, and future, of its multiple councils and committees must be kept in mind. No journal that is the official organ of a medical or other society is or can be a one-man show. Otherwise, it no longer is the official organ.

Not infrequently letters are received that offer protests against a policy of the House of Delegates or a statement by an A. M. A. office. Such letters should be sent to the source of irritation, as only there can the offending policy be changed. This, plus the fact that space is at a premium in THE JOURNAL, prohibits the use of this periodical as an open forum. This does not mean that conflicting viewpoints will not be presented, but they should be confined essentially to scientific matters supportable by the correspondent on request. THE JOURNAL can only report and interpret; it cannot make policy.

One thing always welcome to an editor is a suggestion. It may not be immediately useful, but it is never ignored. THE JOURNAL has incorporated many changes during the last several years. Its format is different, its coverage broader. Much of this came about through suggestions from readers. And the end is not in sight. However, there are many things suggested by or commented on by readers that do not find their way into the pages of THE JOURNAL because the writers do not want publication. In a way this is unfortunate, because the topics merit discussion; for example, one man decries the use of sirens by ambulances on emergency calls. He claims there are few medical indications for ambulances to violate all concepts of common sense safety in a mad dash to hospitals. He is positive that a slower, quieter ride would usually be more beneficial to the patient. As one who was on ambulance call every other night and most days as an intern in a large eastern city the Editor must confess to entertaining the same thoughts as his driver shattered the stillness of the night with raucous screams from the siren.

Another correspondent protests the routine practices in some hospitals whereby patients in a sound sleep are roused to be given sedatives to promote sleep, whereby patients in need of rest are roused two hours before an early breakfast just to have their hands and face washed, whereby floor polishing and other noisy activities are begun even before breakfast, and whereby attendants are allowed to work noisily with garbage cans. The writer especially protests the failure to adopt different policies for different patients, convalescents and the seriously ill being treated alike. He recognizes the needs of the nursing staff and the wishes of the attending physician but denies the need for strict adherence to local rules and customs if common sense can effect more flexible, helpful, and healthful procedures.

And another correspondent takes out after the responsibilities of scientists who accept funds for research. Being aware of the money provided by industry and philanthropic groups, he urges the researcher to assume the same depth of obligation that prospective donors are told to assume. One of his main complaints concerns the failure of some researchers to complete work that they promised to undertake when they asked for and were given funds. Not infrequently his experience has been that these men of science even refused to answer letters seeking information about the progress of the work. When such situations arise they do not make it easier for others to hope for financial support for research.

These are samples only of an editor's correspondence. But his experience is not unique. The same story could be told for practically any office of the Americal Medical Association, for most large national medical and other groups, and for any truly active state or local medical society. Such correspondence is a sign of interest by the members and should not be taken as a source of irritation. As was said above, the mail may be surprising at times but it is never dull.

ORGANIZATION SECTION

EDUCATION BY TELEVISION

President Eisenhower and 13 eminent authorities in the field of coronary disease research attracted an audience of more than 22,000 physicians, residents, interns, and senior medical students to the Feb. 9 Videclinic. The closed-circuit televised postgraduate education program beamed to 32 cities was viewed on large screen receivers in ballrooms and auditoriums. Attendance far exceeded original estimates and resulted in "standing room only" in most Videclinic cities.

President Eisenhower, televised directly from the White House, opened the program by addressing the assembled physicians across the nation. He applauded medical advances that have lengthened the American life span but said, "If the annual toll from coronary artery disease were revealed to the American people as a casualty list from the battlefield the effect would be one of national shock and a demand that something be done. That something *is* being done in such programs as tonight is significant and encouraging."

The President asked the support of physicians in strengthening the agencies of government concerned with the problems of

Doctor Lull described Videclinic as a merging of the science of medicine with the science of electronics to bring medical knowledge directly into the home communities of physicians.

national health. "Yet the role of government in these matters," he continued, "must always be secondary and supplementary. The first responsibility lies with the community determined to foster good health and to provide well for the ailing and the injured; with the scientist as he works in freedom toward goals of his own choosing, and with the physician who brings his healing ministry, not to the state or to the mass of people as such, but always to some man, woman or child—some individual human being worthy of his dedicated care. God speed you on your mission."

The scientific section of the program consisted of live and filmed pick-ups from New York, Boston, Cleveland, Chicago, Minneapolis, and New Orleans. From these cities, Videclinic participants discussed the management of coronary artery disease. In New York, a panel was formed to correlate and expand the televised clinical reports from other cities. Herrman L. Blumgart, Harvard Medical School, moderated the group consisting of E. Cowles Andrus, Johns Hopkins University; Howard B. Burchell, University of Minnesota; Howard P. Lewis, University of Oregon, and Francis C. Wood, Pennsylvania School of Medicine. Reports on coronary disease studies in other cities were made by Paul D. White, National Advisory Heart Council; Frederick J. Stare, Harvard Medical School; Irvine H. Page, Cleveland Clinic; Ancel Keys, University of Minnesota; David P. Barr, Cornell University; Howard B. Sprague, Harvard Medical School; Louis N. Katz, Michael Reese Hospital, Chicago; and George E. Burch, Tulane University.

In closing the "nationwide scientific meeting," George F. Lull, Secretary and General Manager of the American Medical Association, said, "The medical profession today is giving more and more attention to the problem of how to improve and extend postgraduate education. Tonight, by virtue of closed-circuit tele-

Above, President Eisenhower was first to appear on Videclinic theater-size television screens in 32 cities. The President spoke directly from the White House to 22,000 assembled physicians. Below, Drs. Andrus, Burchell, Blumgart, Lewis, and Wood in New York discuss reports of experts in Boston, Cleveland, Minneapolis, Chicago, and New Orleans on the treatment of coronary artery disease.

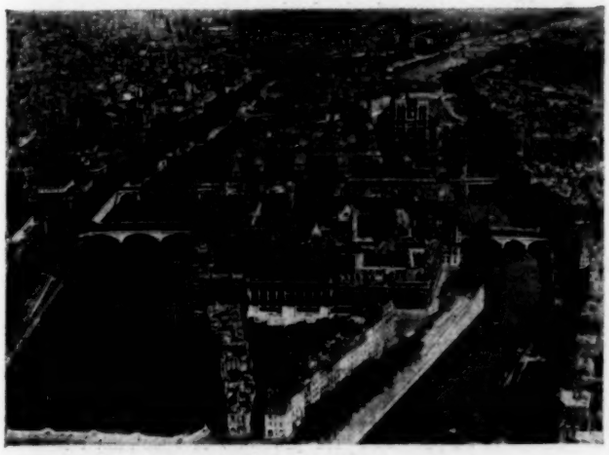
vision, we have been able to break through the limitations of time, distance and seating capacity. The amphitheater has been brought directly to you physicians in your home communities from coast to coast."

The Videclinic was presented jointly by the A. M. A. and local medical societies. It was produced and sponsored by Smith, Kline & French Laboratories of Philadelphia. Cities that received the telecast were selected in areas that would give the maximum number of physicians an opportunity to attend.

PRECONVENTION AND POSTCONVENTION TOURS TO EUROPE

Air tours of Europe, which United Air Lines and Thos. Cook & Son will operate with the consent of the Board of Trustees of the American Medical Association, have been planned to precede and follow the Annual A. M. A. Meeting at Atlantic City, N. J., June 6-10, 1955. The air tours offer a comprehensive itinerary of capital cities and renowned points of interest combined with medical lectures by eminent authorities. Style shows by celebrated designers have been scheduled for the pleasure of the ladies. The four tours, each lasting four weeks, have been planned to meet varied interests and to satisfy the wishes of the most exacting traveler. De luxe air service will be provided by Air France, British Overseas Airway Corporation, El Al Israel, Italian Airlines, K. L. M., Pan American, Sabena Belgian, Scandinavian Airlines System, and Swissair.

Tourists will visit such storied places as Windsor Castle, Westminster Abbey, Pitti Palace, the Colosseum, the Pantheon, Sistine Chapel, Napoleon's Tomb, Tuileries, Palace of Versailles, and Louvre. They will go through Venice in gondolas and see the quaint river towns of Germany from a steamer on the Rhine. Cities to be visited include London, Amsterdam, Haarlem, Hague, Coblenz, Frankfurt, Zurich, Lucerne, Milan, Venice, Florence, Rome, Genoa, Monte Carlo, Grasse, Nice, and Paris.



L'île de la cité, Paris.

Departures from New York are scheduled for May 6, May 8, June 11, and June 13. Those enplaning on May 6 will return to New York on June 3; those enplaning on May 8 will return June 5. Departures of the postconvention tours are set for June 11 and June 13, with return four weeks later.

The cost of the tours is $1,598. This covers round-trip transportation, all meals en route, and hotel accommodations. A deposit of $100 is required at the time of booking. Checks should be drawn to the order of United Air Lines for both the deposit and the final payment, which is due April 8. Requests for booking or additional information should be addressed to the American Medical Association, Pre and Post Convention Tours, 5959 S. Cicero, Chicago 38, Ill. Early application is desirable in order to assure early completion of overseas arrangements.

MEETING OF REHABILITATION TASK FORCE

The first meeting of the Task Force on Rehabilitation, appointed by the A. M. A. Board of Trustees, was held in Washington, Jan. 27-28. The task force consists of Dr. Ralph DeForest, Secretary of the A. M. A. Council on Physical Medicine and Rehabilitation, chairman; George Cooley, associate secretary of the A. M. A. Council on Medical Service; Clark Bridges, assistant to the Secretary of the A. M. A. Council on Industrial Health, and C. Joseph Stetler, Director of the A. M. A. Law Department.

During the two day Washington meeting, conferences were held with K. Vernon Banta of the President's Committee on Employment of the Handicapped, Dr. Leonard Scheele, Dr. W. Palmer Dearing, Dr. Jack Masur, and others of the U. S. Public Health Service, and Miss Mary Switzer and Dr. Joseph Gerber of the Office of Vocational Rehabilitation of the Department of Health, Education, and Welfare. The task force plans to assemble all pertinent material dealing with rehabilitation problems of the local, state, or federal government, as well as rehabilitation activities of nongovernmental groups. The material assembled will be presented to the Board of Trustees with recommendations concerning the position to be adopted by the Association in the field of rehabilitation.

STANDARDS FOR OPERATION OF MEDIATION COMMITTEES

Dr. Dwight H. Murray, Chairman, A. M. A. Board of Trustees, has appointed Dr. J. P. Culpepper, Hattiesburg, Miss., as chairman of a committee that will study and report on recommended standards for the operation of mediation committees. Other committee members are Drs. George A. Unfug, Pueblo, Colo.; Frank D. Costenbader, Washington, D. C.; Kenneth H. Frankhauser, Avon, Ill.; and Cleon A. Nafe, Indianapolis.

The committee was appointed in keeping with two resolutions introduced in the House of Delegates at the Miami meeting. The two resolutions requested the Board of Trustees to "appoint a nationally representative special committee, to consist of representatives of successful mediation or grievance committees howsoever they may be entitled in the various states, to study this problem and recommend through the Board of Trustees to the House of Delegates such standards as may be promulgated by the American Medical Association as a guide to the organization and functioning of such bodies in the constituent associations and component societies." Dr. Culpepper said that every effort would be made to have at least a progress report ready for the Board before the A. M. A. Atlantic City meeting in June.

FEDERAL MEDICAL LEGISLATION

Fourth Installment, First Session, 84th Congress

Tax Postponement for the Self-Employed

Congressman Ray (R., N. Y.), in H. R. 2092, has again introduced a measure "to encourage the establishment of voluntary pension plans by individuals." For the purpose of income tax he would allow the deduction from the gross income of "amounts paid into a restricted retirement fund, or to a life-insurance company as premiums under a restricted retirement annuity contract." According to the bill this amount for a taxable year shall not exceed the lesser of—

(A) 2½ percent of the taxpayer's earned adjusted gross income from covered sources plus 5 percent of his earned adjusted gross income from all other sources, or

(B) $1,000 in the case of a taxable year beginning after December 31, 1955, and ending before July 1, 1957; $2,000 in the case of a taxpable year ending after June 30, 1957, and before July 1, 1958; and $3,000 in the case of a taxable year ending after June 30, 1958.

"Covered" income for the purposes of the bill means income from a corporation, association, or governmental unit that contributes to a recognized pension or retirement plan. The self-employed would be allowed a 5% deduction. There is a special arrangement for those who become 50 years of age before Jan. 1 to build up their retirement at a faster rate by increased deductions but not in excess of 20% of the adjusted gross income. Provision is made for carrying over a limited amount of unused exclusions. A number of essentially similar bills have been introduced: H. R. 2103, Bosch (R., N. Y.); H. R. 2143, Kearney (R., N. Y.); H. R. 2154, Latham (D., Ga.); and H. R. 2221, Wainwright (R., N. Y.). The above bills were referred to the Ways and Means Committee.

Medical Tax Deduction

Congressman Hand (R., N. J.), in H. R. 1799, would allow deductions for income tax purposes of contributions or gifts to certain prepayment health services plans as credit against actual income tax itself. A variable amount would be allowed depending on the adjusted gross income.

Prepared by the Washington Office of the American Medical Association.

(1) if the adjusted gross income of the taxpayer is $2,000 or under, 90 per centum of the amount paid:

(2) if the adjusted gross income of the taxpayer is between $2,001 and $4,000, 85 per centum of the amount paid;

(3) if the adjusted gross income of the taxpayer is between $4,001 and $6,000, 80 per centum of the amount paid;

(4) if the adjusted gross income of the taxpayer is between $6,110 and $8,000, 75 per centum of the amount paid;

(5) if the adjusted gross income of the taxpayer is between $8,001 and $10,000, 70 per centum of the amount paid; and

(6) if the adjusted gross income of the taxpayer is $10,001, or over, 60 per centum of the amount paid.

This bill was referred to the Ways and Means Committee.

Incorporation of American Federation of the Physically Handicapped

Senators Langer and Young (R., N. D.), in S. 529, would grant a federal charter to the American Federation of the Physically Handicapped. Among the purposes of the corporation would be to "foster, encourage, and promote methods and procedures leading to increased rehabilitation and employment of our millions of physically and mentally handicapped citizens." This bill was referred to the Judiciary Committee.

Doctor Draft Extension

Congressman Vinson (D., Ga.), chairman of the Armed Forces Committee, has introduced a proposal for the extension of the doctor draft. H. R. 2886 would extend until July 1, 1957, the "Doctor-Draft" act of 1950 as amended. This bill was referred to the Armed Services Committee.

Medical Care for Veterans Residing in the Philippines

Congressman Bentley (R., Mich.) proposes, in H. R. 2001, to authorize the Administrator of Veterans' Affairs "to enter into such contracts and other arrangements as he deems necessary in order to provide hospital, medical and domiciliary care, including treatment, in the Republic of the Philippines to veterans entitled thereto." This bill was referred to the Veterans' Affairs Committee.

Amending Longshoremen's and Harbor Worker's Compensation Act

Congressman Tollefson (R., Wash.) proposes, in H. R. 2032, to amend the Longshoremen's and Harbor Worker's Compensation Act to provide "that an injured employee should have the right to select his own physician." This right was limited somewhat. An employer is given a limited right to transfer medical care to another physician. The deputy commissioner is given authority to declare ineligible any physician who "has been guilty of professional misconduct or other incompetency in connection with services rendered." General costs would be paid by the employer and subject to his supervision and approval. This bill was referred to the Committee on Education and Labor.

Promotion in the Armed Services

Congressman Brooks (D., La.) has introduced a measure, H. R. 2108, that would repeal provisions requiring professional examinations of medical, dental, and veterinary officers for promotion but would retain physical examinations. This bill was referred to the Armed Services Committee.

Air Pollution

Congressman Frelinghuysen (R., N. J.), in H. R. 2129, would authorize the appropriation of 5 million dollars "to provide for intensified research into the causes, hazards, and effects of air pollution, and the methods for its prevention and control." The Secretary of the Department of Health, Education, and Welfare would administer the program and could contract with state and local governments, educational institutions, and other nonprofit organizations to make appropriate studies. This measure is identical with H. R. 835 by Ray (R., N. Y.). This bill was referred to the Interstate and Foreign Commerce Committee.

Administration Health Omnibus Bill

The administration omnibus health bill was introduced in the Senate by: Smith (R., N. J.) for himself, Ives (R., N. Y.), Purtell (R., Conn.), Bender (R., Ohio), Allott (R., Colo.), Thye (R., Minn.), Bush (R., Conn.), Saltonstall (R., Mass.), Case (R., N. J.), Duff (R., Pa.), and Watkins (R., Utah).

In the House, Mr. Priest, in H. R. 3458, introduced the identical measure. The purpose was stated as follows: "To improve the health of the people by encouraging the extension of voluntary prepayment health services plans, facilitating the financing of construction of needed health facilities, assisting in increasing the number of adequately trained nurses and other health personnel, improving and expanding programs of mental health and public health, and for other purposes."

Reinsurance.—The section on reinsurance is similar to the reinsurance bills in the last Congress, H. R. 8356 and S. 3114. The federal government would put up an initial 25 million dollars to start a fund for reinsuring selected health services plans, providing the plans agree to experiment with new types or scopes of coverage. Cited particularly are the coverage of farm and low-income families and the extension of insurance to provide home and office medical costs and larger medical costs. Participation in the plan would be voluntary and the premiums would be assessed, an amount to be used in a revolving fund to pay 75% of the excessive losses in selected plans. The plan would theoretically be self-sustaining, and 25 million dollars would be made available by the government at the start and eventually be repaid. The authorized limit, however, for this fund would be 100 million dollars.

Mortgage Loan Insurance.—The corporations or individuals who could obtain a guaranteed loan would be widened to include, besides nonprofit institutions, profit-making hospitals, clinics, nursing, and convalescent homes. The requirement that 60% of the insured medical facility be reserved for serving members of group practice prepayment health plans has been eliminated. To be eligible for insurance the loan by the private lender could not exceed 80% of the estimated value. The reinsurance would not exceed 95% of the loan, and the loan could not exceed 30 years. Remodeling or expansion would be included.

Practical Nurse Training.—Additional vocational training grants would be authorized to be distributed through the Office of Education to states over a five year period to stimulate the training of practical nurses on a less than college grade. The state administration would be through the state board of vocational education or the state board with primary responsibility in this field.

Graduate Training of Professional Nurses and Public Health Personnel.—Scholarships would be provided to train graduate nurses for teaching and supervisory work. Scholarships (traineeships) would be provided "for graduate or specialized training in public health for doctors, engineers, nurses, and other professional health personnel." This section would be administered by the Public Health Service.

Grants to States for Public Health Services.—The section on grants to states for public health services would replace the present separate categorical disease control grants with three new types of grants: (1) a general authorization for public health services, (2) grants to insure the extension and improvement of these services, and (3) grants for special projects. Mental health is covered in a new enlarged program (see below). Under the proposal the states would have two years to become adjusted to the new system. During this period every state would be allocated the same amount of money it is receiving this fiscal year, including funds for cancer control. Any appropriation remaining would be distributed to states under the new formula, which would take into account the relative financial needs of the state and the extent of the particular health problems, as well as the state's population. After two years, all funds would be allocated on this need-population-per-capita-income formula.

Mental Health.—The section on mental health would authorize an expanded five year program of grants to states and direct assistance to projects in the field of mental health. Money would be allocated to states on a need-population-per-capita-income formula. Included would be instruction of personnel and cost of administration. The Surgeon General of the Public Health Service would administer the program and could use a special appropriation to develop improved methods of care, treatment, and rehabilitation of the mentally ill and could make grants to individuals, private as well as public agencies, and to states for this purpose. This bill was referred to the Committee on Labor and Public Welfare in the Senate and to the Interstate and Foreign Commerce Committee in the House.

MEDICAL NEWS

CALIFORNIA

Physicians' Art Exhibition.—The annual exhibition of the Los Angeles Physicians' Art Society will be held March 30-April 16 at the Los Angeles County Medical Association Building, 1925 Wilshire Blvd., Los Angeles. Physicians are invited to send their exhibits no later than 5 p. m., March 25, to the association's headquarters. An exhibitor may submit as many pieces as he desires, but no more than three will be selected for exhibit. A hanging charge will be made, and only duly paid members may submit exhibits. The exhibition will open with a cocktail party and buffet dinner ($3 per plate) at 6:30 p. m., March 30. Family and friends are invited.

Medical Electronics Fellowship.—The electrical engineering department of Stanford University, Stanford, announces a graduate fellowship in medical electronics open to a man with a major interest in electronics coupled with an interest in medicine or biology. The candidate will normally have a bachelor's degree in electrical engineering or physics. He will be expected to pursue work in electronics leading to an advanced degree, together with appropriate studies in medicine, biology, and chemistry. This award is made possible by a grant from the Hewlett-Packard Company in Palo Alto. Research already under way at Stanford includes work on an accelerator for medical use, analysis of animal and vegetable specimens by nuclear resonance, x-ray microscopy, and the transmission of electrical impulses along nerve fibers. A professional group on medical electronics of the Institute of Radio Engineers holds meetings frequently in the area. The fellowship will carry an annual stipend of $1,800 to $2,500, depending on qualifications. Candidates should apply to the Assistantship and Fellowship Committee of the Electrical Engineering Department at Stanford on forms provided by the department. Applications to be considered for the school year 1955-1956 should be in by April 1.

COLORADO

Postgraduate Pediatric Course.—"The Clinical Management of Emotional Problems in Children" is the theme of a postgraduate conference for physicians to be presented at the University of Colorado Medical Center, 4200 E. Ninth Ave., Denver, April 4-9, under the sponsorship of the University of Colorado School of Medicine; the departments of pediatrics, psychiatry, and human growth; the office of postgraduate medical education; and the Colorado State Department of Public Health. At each session Dr. Reginald S. Lourie, director, Psychiatric Clinic, The Children's Hospital, Washington, D. C., will present a 30 to 45 minute discussion, illustrated with abstracts of clinical cases. Dr. Lourie will also demonstrate a representative psychiatric interview with a patient and will be the speaker at the dinner meeting of the Rocky Mountain Pediatric Society at the University Club, 1673 Sherman, Wednesday, 7 p. m.

CONNECTICUT

Cancer Conference.—The Connecticut Cancer Conference for Physicians announces two symposiums on the most common cancers in persons in Connecticut. Dr. Richard B. Cattell, director, Lahey Clinic, Boston, will serve as moderator for "Cancer of the Colon," and Dr. Cushman D. Haagensen, associate professor of clinical surgery, Columbia University College of Physicians and Surgeons, New York, for "Cancer of the Breast." The meeting will be at the Hotel Taft, New Haven, March 23, 1 to 5:45 p. m., under the co-sponsorship of the Connecticut Division, American Cancer Society; Association of Connecticut Tumor Clinics; Connecticut State Medical Society; and Connecticut State Department of Health. Members of the Academy of General Practice will be granted postgraduate credit for attendance at this conference.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

ILLINOIS

Tuberculosis Conference.—The sixth annual tuberculosis conference, sponsored by the Tuberculosis Institute of Chicago and Cook County, March 24-25, will be at the Hotel Sherman, Chicago. Among the speakers will be Dr. Julius L. Wilson, associate director, Henry Phipps Institute, Philadelphia; Dr. Edward T. Blomquist, medical director, tuberculosis program, Department of Health, Education, and Welfare, Washington, D. C.; Dr. Nicholas D. D'Esopo, chief of tuberculosis service, Veterans Administration Hospital, West Haven, Conn.; Dr. Edith H. M. Lincoln, professor of clinical pediatrics, New York University College of Medicine; Dr. Harold M. Graning, regional medical director, United States Public Health Service, Chicago; and Dr. Sidney H. Dressler, medical director, National Jewish Hospital, Denver. Among the topics to be considered are medical socioeconomic aspects of tuberculosis control; chemotherapy; treatment of primary tuberculosis in children; and education in hospitals and clinics. On Friday there will be discussion on legislation requiring compulsory chest roentgenograms and compulsory isolation of the recalcitrant tuberculosis patient. Dr. Jerome R. Head, medical director, Edward Sanatorium, Naperville, and Dr. Winston H. Tucker, commissioner of health, Evanston, will present the two points of view.

Chicago

Union Opens New Health Center.—The A. F. L. International Ladies Garment Workers Union has opened its new $250,000 Health Center at 6 S. Wacker Dr. Equipped with laboratories, x-ray rooms, and a room for minor surgery, it is designed to serve 10,000 workers. Construction was financed by the garment industry's contributions of 0.5% of the entire payroll to a fund, controlled jointly by union and employer trustees. The cost of maintaining the center is about $140,000 annually. Dr. Stanley E. Telser has been named director; he will be aided by a staff of physicians, technicians, and nurses.

MARYLAND

Kolson Memorial Lecture.—The Dr. Jack W. Kolson Memorial Lecture sponsored by the house staff of Sinai Hospital, Baltimore, will be delivered at 8:30 p. m. March 24 in Hurd Hall, Johns Hopkins Hospital, Baltimore, by Dr. G. Lyman Duff, Strathcona Professor of Pathology and dean of the McGill University Faculty of Medicine, Montreal, Canada, whose subject will be "The Pathogenesis of Atherosclerosis and Current Concepts of Treatment."

MASSACHUSETTS

Examining Physicians Meet in Boston.—The yearly meeting of the Massachusetts Society of Examining Physicians will be held at the Harvard Club, Boston, March 23. A social hour will precede supper at 7 p. m. The speaker for the evening will be Dr. Robert T. McElvenny, Chicago, associate professor of bone and joint surgery, Northwestern University Medical School. Dr. McElvenny's subject will be "The Rise and Decline of Medical Expense and Hospital Costs." Members of the Massachusetts Hospital Association are invited.

MISSISSIPPI

Institute on Oral Cancer.—An institute on oral cancer will be held March 23 at the University of Mississippi in University; March 24 at Millsaps College in Jackson; and March 25 at Gulfport Park College in Gulfport, under the sponsorship of the Mississippi Dental Association, the Mississippi State Medical Association, the University of Mississippi, American Cancer Society, and the Mississippi state boards of health, dental ex-

aminers, and medical examiners. All professional persons interested in oral cancer are invited to the meetings, which will begin with a general consideration of the problems of malignancy. Among the speakers will be Emanuel Cheraskin, M.D., D.M.D., associate professor of oral diagnosis and oral medicine; Leonard Robinson, M.D., D.M.D., associate professor of oral pathology; and Joseph P. Lazansky, M.D., D.D.S., D.M.D., chairman, department of oral medicine, oral surgery, and oral pathology, University of Alabama School of Dentistry in University. There will be an open discussion period.

MISSOURI

State Medical Meeting.—The 97th annual session of the Missouri State Medical Association will be held in the Municipal Auditorium and the Hotel President, Kansas City, March 27-30, under the presidency of Dr. Harold E. Petersen, St. Joseph. Daily color television programs will open the sessions at 8:30 a. m. Monday at 10:30 a. m. Dr. Elmer Hess, Erie, Pa., A. M. A. President-Elect, will discuss "Management of Cancer of the Prostate." Dr. Hess will be the speaker at the banquet Tuesday, 7:30 p. m., when his topic will be "What's Right with Medicine?" Presentations by other out-of-state speakers include:

Treatment of Hypertension, Irvine H. Page, Cleveland.
The Acute Abdomen, Philip Thorek, Chicago.
Effect of Mitral Valve Surgery on the Prognosis of Individuals with Mitral Stenosis, Louis A. Soloff, Philadelphia.
Acute Renal Insufficiency (Lower Nephron Nephrosis), Francis D. Murphy, Milwaukee.
Chest X-Ray in the Diagnosis of Lung Cancer, L. Henry Garland, San Francisco.
Diabetes in Children: Prevention of Complications, Priscilla White, Boston.
Cancer: An Evaluation of Surgical Treatment, George Crile, Cleveland.

Luncheons will be held Monday and Tuesday, 12 noon, at the Hotel President.

NEW YORK

Society News.—The Medical Society of the County of Erie will hold its fourth annual joint good fellowship meeting with the Erie County Pharmaceutical Association at the Hotel Statler, Buffalo, in the evening of March 22. Dr. Dale Gilbert Friend, associate in medicine on the faculty of Harvard Medical School, Boston, will present "Observations on Some of the Newer Drugs." A collation and social hour will end the evening session.

Miller Memorial Lecture.—The first Dr. George I. Miller Memorial Lecture will be given by Dr. Joseph Pick, associate professor of anatomy at the New York University College of Medicine, New York City. The lecture, "Clinical Aspects of the Autonomic Nervous System," jointly sponsored by the departments of anesthesiology and surgery of the Unity Hospital, Brooklyn, will be presented at the hospital, 1545 St. John's Place, at 8:30 p. m., March 24.

New York City

Ross Golden Lecture.—Dr. Eugene P. Pendergrass, Philadelphia, will deliver the second Ross Golden Lecture before the New York Roentgen Society March 21, 8:30 p. m., at the New York Academy of Medicine. His topic will be the roentgen diagnosis of silicosis and the responsibility of the radiologist.

Goldforb Lectureship.—The third annual lecture in honor of Abraham J. Goldforb, Ph.D., will be sponsored by his students and colleagues March 21, 8:30 p. m., at the New York Academy of Medicine Building, Fifth Avenue at 103rd Street. The introduction by Dr. Lloyd F. Craver, professor of clinical medicine, Cornell University Medical College, will be followed by "Progress in Cancer Research" by Dr. Cornelius P. Rhoads, scientific director, Memorial Center for Cancer and Allied Diseases.

Society News.—At the meeting of the Society for the Study of the Blood, March 22, 8:30 p. m., in the New York Academy of Medicine, 2 E. 103rd St., Dr. Benjamin Alexander, associate professor of medicine, Harvard Medical School, Boston, will discuss "Current Concepts in the Coagulation Mechanism," and Dr. Martin C. Rosenthal, assistant attending hematologist, the Mount Sinai Hospital, will have as his topic "The Diagnosis and Treatment of the Disorders of Coagulation."——An institute on alcoholism, open to physicians only, will be held at the Hotel Statler, 33rd Street and Seventh Avenue, March 19. Papers will be read by Drs. Ebbe C. Hoff, Richmond, Va.; Arnold Z. Pfeffer, New York; and Anthony Zappala, Washington, D. C.

OREGON

Course for Otolaryngologists.—The University of Oregon Medical School, Portland, has arranged a course, "The Reconstruction of the Nasal Septum and External Pyramid," which will be presented to 21 otolaryngologists from four states, Canada, Hawaii, and Australia March 19-26. Dr. Maurice H. Cottle, head, department of otolaryngology, Chicago Medical School, will supervise the program, which includes seminars and panel discussions. In addition, 15 patients will undergo surgery on the nose, which is to be performed before the classes in Multnomah Hospital, Portland. An exhibition of various phases of otolaryngology set up by the instructors in the anatomy laboratory and a lecture by Dr. Cottle at 7 p. m. Wednesday in the school auditorium are events open to the faculty, students, and community. The faculty of the course includes specialists from Oregon, California, Utah, Colorado, Wyoming, Missouri, Texas, Indiana, Illinois, Ohio, Michigan, Kentucky, Louisiana, North Carolina, Maryland, New York, Pennsylvania, Connecticut, and British Columbia, Canada.

PENNSYLVANIA

Annual Postgraduate Institute.—The Philadelphia County Medical Society will hold its 19th annual Postgraduate Institute at the Bellevue-Stratford Hotel, March 29-April 1. Subjects to be considered are hypertension, laboratory tests, thyroid disease, advances in anesthesia and roentgenology, undesirable side-effects of drugs, common deformities, coronary artery disease, immunization in children, emotional implications of aging, diseases of the eye, and infertility. The director of the institute is Dr. Leandro M. Tocantins, Philadelphia. The registration fee for nonmembers is $10. Guest presentations include:

Dickinson W. Richards, New York, Forms of Pulmonary Insufficiency Secondary to Chronic Disease of the Lungs.
James J. Nickson, New York, Relative Merits of Supervoltage Therapy, Including Cobalt Bomb, and Conventional 200-250 KV Radiation in the Treatment of Malignant Tumors.
David Gitlin, Boston, Agammaglobulinemia.
John C. Locke, Montreal, Canada, Retrolental Fibroplasia.
John Rock, Boston, Infertility.
Henry T. Bahnson, Baltimore, Surgical Treatment of Aortic Aneurysms.

There will be a symposium on the thyroid Wednesday afternoon and panel discussions on pediatric immunization and on emotional implications of the aging Thursday afternoon. Scheduled for Wednesday evening are a dinner and entertainment (dress optional) and for Thursday evening a clinical pathological conference.

Philadelphia

Annual Course on Pediatrics.—The division of pediatrics of the Hahnemann Medical College and Hospital of Philadelphia will present its annual postgraduate course, "Pediatrics for the General Practitioner," each Wednesday from March 16 to June 1. This course, approved by the American Academy of Pediatrics, emphasizes progress in handling the problems of infancy and childhood met by the general practitioner. Clinical material will be used whenever possible. Classes (limited to 25 students) will meet in the seventh floor classroom of the Hahnemann Hospital, 230 N. Broad St.

TENNESSEE

Jackson Clinic's Annual Seminar.—The Jackson Clinic of Jackson will hold its second annual seminar at the clinic on March 27. Physicians from the surrounding area are invited to the meetings and luncheon. Speakers are Drs. Robert H. Barker, associate professor of obstetrics and gynecology, and Richard Warren, associate professor of surgery, Harvard Medical School, Boston. During the morning, "Management of Breech Presentation" and "Management of Acute Arterial Obstruction" will be discussed. The afternoon topics are "Management of Uterine Bleeding" and "Surgical Aspects of Venous Stasis in the Leg."

TEXAS

Meyer Bodansky Lecture.—Dr. Ephraim Shorr, professor of internal medicine at Cornell University Medical College, New York, and director, special metabolic service, New York Hospital, will give the annual Meyer Bodansky Lecture at the University of Texas Medical Branch, Galveston, 4 p. m., March 21, on "The Intermediary Metabolism and Biological Activities of Ferritin." The Meyer Bodansky Lectureship, which will be presented by the Alpha Nu chapter of Phi Delta Epsilon fraternity, honors the late Dr. Meyer Bodansky (1896-1941) who was professor of pathological chemistry at the medical branch from 1920 to the time of his death.

VIRGINIA

Postgraduate Day Program.—The staff of the Memorial and Crippled Children's Hospital, Roanoke, will hold its sixth annual postgraduate day program March 23 at the Hotel Roanoke. Registration at 1 p. m. will be followed by presentation of "Surgery of Mitral Valvular Disease," by Dr. Lewis H. Bosher Jr., Medical College of Virginia, Richmond, and "Surgical Timing and Prognosis of Congenital Heart Disease," by Dr. J. Francis Dammann Jr., University of Virginia Department of Medicine, Charlottesville. A clinical-pathological conference will then be conducted by Dr. W. Proctor Harvey, Georgetown University School of Medicine, Washington, D. C. (clinician) and Dr. James C. Gale, Memorial and Crippled Children's Hospital (pathologist), after which Dr. Harvey will serve as moderator for a panel discussion, "Problems in Pre- and Post-Operative Care," with Drs. Bosher, Dammann, and Elliot V. Newman, Vanderbilt University School of Medicine, Nashville, Tenn., as collaborators. Following the afternoon session, there will be a social hour, banquet, and after-dinner lecture, "The Basic Mechanisms and Clinical Classification of Heart Failure," by Dr. Newman.

WASHINGTON

New Clinic Program at Orthopedic Hospital.—A clinic for the child amputee will be held the second Thursday of every month at the Children's Orthopedic Hospital, Seattle, as part of the Upper Extremity Field Study Program of New York University, supported by the National Research Council. Children referred to the program will be studied by a team consisting of Dr. Ernest M. Burgess, orthopedic surgeon; Mr. Russell Brain, consultant in artificial limbs, and Miss Barbara Fassett, physical therapist. The hospital's social service department will also give assistance. This team will evaluate the needs of the child amputee, prescribe the artificial limb, and teach the young patient in its use. Results of findings in the new program at the Children's Orthopedic Hospital will be compared with those of other participating agencies throughout the nation.

Obstetrical Meeting.—The Washington State Obstetrical Association will meet March 26 at the Multnomah Hotel, Portland, Ore. Dr. Norman F. Miller, professor of obstetrics and gynecology, University of Michigan Medical School, Ann Arbor, will discuss "Terminal Care of the Gynecologic Cancer Patient" and "Handmaiden to Maternal Assassins." Dr. F. Bayard Carter, professor of obstetrics and gynecology, Duke University School of Medicine, Durham, N. C., will have as his topics "Pregnancy Complicated by Cancer of the Cervix" and "Vaginal Approach to Pelvic Pathology." Dr. Howard C. Stearns, professor of obstetrics and gynecology, University of Oregon Medical School, Portland, will be moderator of the luncheon round-table discussion. Dr. Laurence Selling, professor emeritus of medicine, University of Oregon Medical School, will speak at the banquet. Registration must be made in advance and accompanied by a check for the fee: $8 for members and $11 for nonmembers. Information may be obtained from the Washington State Obstetrical Association, 805 Medical-Dental Building, Seattle 1.

WISCONSIN

Course in Internal Medicine.—The University of Wisconsin Medical School, Madison, offers a postgraduate course in internal medicine March 29-31. Dr. Ovid O. Meyer, professor and chairman of the department of medicine, will conduct the course. The registration fee is $5; the course fee, $15. Application for registration should be sent to Dr. Robert C. Parkin, University of Wisconsin Medical School, 418 Randall Ave., Madison 6.

GENERAL

Allergists Meet in Florida.—The Southeastern Allergy Association will meet at the Orange Court Hotel, Orlando, Fla., March 25-26, to discuss "Allergy and Its Relation to Industrial Medicine."

Cancer Conference at Wichita.—The seventh annual Mid-West Cancer Conference will convene March 24-25 at the Broadview Hotel, Wichita, Kan., under the sponsorship of the American Cancer Society, Kansas Division, and the Kansas Medical Society. Guest speakers include: Drs. Richard H. Chamberlain and J. Herbert Nagler, Philadelphia; Dr. Elson B. Helwig, Washington, D. C.; Clarence C. Little, Sc.D., Bar Harbor, Me.; Dr. John R. McDonald, Rochester, Minn.; Dr. Robert D. Moreton, Fort Worth, Texas; Dr. George T. Pack, New York; and Dr. Henry K. Ransom, Ann Arbor, Mich.

Conference on Anesthesiology.—The biennial Western Conference on Anesthesiology at the Hotel Mark Hopkins, San Francisco, March 21-23, will have as its theme "Endocrines and Enzymes." Dr. Edgar A. Pask of the department of anesthesiology, University of Durham Medical School, Newcastle-Upon-Tyne, England, will serve as moderator. The following panel discussions have been scheduled: Use and Abuse of Intravenous-Inhalant-Relaxant Combinations in Anesthesia; Anesthesia and the Stress Syndrome; Problems in Anesthesia and Surgery of the Ductless Glands; and Care of the Old, the Ill, and the Exhausted in the Operating Room. Dr. M. Dighy Leigh, Los Angeles, will be chairman for a symposium on metabolism depression Wednesday afternoon.

General Practitioners Meet in Los Angeles.—The American Academy of General Practice will hold its annual scientific assembly at the Statler Hotel, Los Angeles, March 28-31 under the presidency of Dr. William B. Hildebrand, Menasha, Wis. Among the speakers will be Dr. Alton Ochsner, New Orleans; Dr. Julian P. Price, Florence, S. C.; Dr. Charles P. Larson, Tacoma, Wash.; Dr. Edith W. Potter, Chicago; Drs. M. Digby Leigh and Lowell S. Goin, Los Angeles; Mr. Eddie Wojecki, Rice Institute, Houston, Texas, head trainer of the 1952 American Olympic team; and Mr. Lynn O. Waldorf, head football coach, University of California, Berkeley. The following panels have been scheduled: Monday, 1:30 p. m., Preserving the Doctor's Life and Usefulness, Dr. Malcolm Phelps, El Reno, Okla., moderator; Tuesday, 9 a. m., Diabetes, Dr. DeWitt K. Burnham, San Francisco, moderator; 2:30 p. m., Childhood Disasters, Dr. E. Keith Hammond, Paoli, Ind., moderator; Wednesday, 9 a. m., Medical and Surgical Aspects of Peripheral Vascular Diseases, Dr. Hugh H. Hussey, Washington, D. C., moderator; 11 a. m., Endocrinology, Dr. Randall G. Sprague, Rochester, Minn., moderator; 1:30 p. m., Neurology, Dr. William Parson, Charlottesville, Va., moderator; and Thursday, 9 a. m., Handling the Athletic Injury, Dr. James T. Harkness, Berkeley, Calif., moderator. The state officers' dinner will be on Monday evening; the congress of delegates' dinner on Tuesday; and the president's reception Wednesday evening. A special train for Los Angeles will leave the Union Station in Chicago, March 23. It may be boarded at Omaha, Denver, and at Salt Lake City, where the entire day will be spent in sight-seeing. The 16 day trip will include preconvention stops in Las Vegas and Boulder Dam and postconvention visits in San Francisco and the Grand Canyon.

LATIN AMERICA

Neurosurgical Congress.—The sixth Latin-American Neurosurgical Congress will be held in Montevideo, Uruguay, March 21-24, during which time the second South American Electroencephalographical Congress will also convene. Official reports will be made on cisternal herniations, pain surgery, and dyskinesias. A symposium on the thalamus will have as discussants Horace W. Magoun, Ph.D., Los Angeles, and Dr. Percival Bailey, Chicago.

FOREIGN

Invitation to Nassau.—With the agreement of the chief medical officer of the Bahama Islands, facilities will be provided for lectures and clinical demonstrations at the New Bahamas General Hospital for physicians who spend their holidays in Nassau. In addition, an auditorium will be available, situated in the gardens of the British Colonial Hotel next to its own private beach. Beginning April 1, arrangements have been made enabling physicians and their families to stay in Nassau at the British Colonial Hotel at especially reduced rates, and some of the principal air lines have agreed to offer special arrangements. Aside from the registration fee of $50 for participation in the postgraduate assemblies, there are no other fees. Information may be obtained from Dr. B. L. Frank, 1290 Pine Ave., West, Montreal, Canada.

Congresses in Internal Medicine.—In its seminar congresses in internal medicine the American Medical Society of Vienna will present the following programs by the medical faculty of the University of Vienna:

April 7-9, Allergy—Arthritis.
May 5-7, Heart Diseases; Cardiovascular Diseases; Peripheral Vascular Diseases.
June 2-4, Cardiology; Electrocardiology; Vectocardiography-Ballistocardiography.
July 7-9, Diabetes; Liver and Biliary Tract Diseases; Hypertension and Nephritis.
August 4-6, Endocrinology; Metabolism; Fluid and Electrolyte Balance.
Sept. 1-3, Gastroscopy; Gastroenterology; Proctology.
Oct. 6-8, Hematology; Normal Peripheral Blood and Bone Marrow; Diseases of Blood and Blood Forming Organs.
Nov. 3-5, Diseases of the Chest; Tuberculosis; Malignant Diseases.

Details may be obtained from the American Medical Society of Vienna, I. Vienna, Universitaetsstrasse 11. Gable: "Ammedic" Vienna.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1955 Annual Meeting, Atlantic City, N. J., June 6-10.

1955 Clinical Meeting, Boston, Nov. 29-Dec. 2.

1956 Annual Meeting, Chicago, June 11-15.

1956 Clinical Meeting, Seattle, Nov. 27-30.

1957 Annual Meeting, New York, June 3-7.

AERO MEDICAL ASSOCIATION, Hotel Statler, Washington, D. C., March 21-23. Dr. Thomas H. Sutherland, P. O. Box 26, Marion, Ohio, Secretary.

ALABAMA, MEDICAL ASSOCIATION OF THE STATE OF, Whitley Hotel, Montgomery, April 21-23. Dr. Douglas L. Cannon, 537 Dexter Ave., Montgomery, Secretary.

AMERICAN ACADEMY OF GENERAL PRACTICE, Los Angeles, March 28-31. Mr. Mac F. Cahal, 406 West 34th St., Kansas City, Mo., Executive Secretary.

AMERICAN ACADEMY OF NEUROLOGY, Shamrock Hotel, Houston, Tex., April 28-30. Dr. Alexander T. Ross, Indiana University Medical Center, Indianapolis 7, Secretary.

AMERICAN ACADEMY OF PEDIATRICS, Spring Session, Sheraton-Cadillac Hotel, Detroit, April 4-7. Dr. E. H. Christopherson, 610 Church St., Evanston, Ill., Executive Secretary.

AMERICAN ASSOCIATION OF ANATOMISTS, Philadelphia, April 6-8. Dr. N. L. Hoerr, 2109 Adelbert Rd., Cleveland 6, Secretary.

AMERICAN ASSOCIATION FOR CLEFT PALATE REHABILITATION, Statler Hotel, Boston, May 13-14. Dr. Jack Matthews, 1617 Cathedral of Learning, University of Pittsburgh, Pittsburgh 13, Secretary.

AMERICAN ASSOCIATION FOR HEALTH, PHYSICAL EDUCATION AND RECREATION, Hotel Statler, Boston, April 17-20. Mr. William F. Meredith, Dept. of Physical Education, University of Pennsylvania, Philadelphia 4, Secretary.

AMERICAN ASSOCIATION OF THE HISTORY OF MEDICINE, Hotel Park Shelton, Detroit, May 12-14. Dr. Samuel X. Radbill, 7043 Elmwood Ave., Philadelphia 42, Secretary.

AMERICAN ASSOCIATION OF IMMUNOLOGISTS, San Francisco, April 10-16. Dr. F. S. Cheever, University of Pittsburgh School of Public Health, Pittsburgh 13, Secretary.

AMERICAN ASSOCIATION OF PATHOLOGISTS AND BACTERIOLOGISTS, The Shamrock, Houston, Texas, April 7-9. Dr. Edward A. Gall, Cincinnati General Hospital, Cincinnati 29, Secretary.

AMERICAN ASSOCIATION OF RAILWAY SURGEONS, Drake Hotel, Chicago, April 12-14. Dr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Secretary.

AMERICAN ASSOCIATION FOR THE STUDY OF NEOPLASTIC DISEASES, Lord Baltimore Hotel, Baltimore, April 28-30. Dr. Bruce H. Sisler, P. O. Box 268, Gatlinburg, Tenn., Secretary.

AMERICAN ASSOCIATION FOR THORACIC SURGERY, Chalfonte-Haddon Hall, Atlantic City, N. J., April 24-26. Dr. Paul C. Samson, 3959 Happy Valley Rd., Lafayette, Calif., Secretary.

AMERICAN COLLEGE OF ALLERGISTS, Morrison Hotel, Chicago, April 25-30. Dr. Fred W. Wittich, 401 LaSalle Med. Bldg., Minneapolis 2, Secretary.

AMERICAN COLLEGE OF PHYSICIANS, Benjamin Franklin and Bellevue-Stratford Hotels, Philadelphia, April 25-29. Mr. E. R. Loveland, 4200 Pine St., Philadelphia 4, Executive Secretary.

AMERICAN DERMATOLOGICAL ASSOCIATION, Bellevue-Biltmore Hotel, Belleair, Fla., April 17-21. Dr. J. Lamar Callaway, Duke Hospital, Durham, N. C., Secretary.

AMERICAN FEDERATION FOR CLINICAL RESEARCH, Haddon Hall, Atlantic City, N. J., May 1. Dr. Lawrence E. Hinkle Jr., 525 East 68th St., New York 21, Secretary.

AMERICAN GERIATRICS SOCIETY, Hotel Roosevelt, New York, April 21-22. Dr. Malford W. Thewlis, 25 Mechanic St., Wakefield, R. I., Secretary.

AMERICAN GOITER ASSOCIATION, Skirvin Hotel, Oklahoma City, April 28-30. Dr. John C. McClintock, 149½ Washington Ave., Albany 10, N. Y., Secretary.

AMERICAN PHYSIOLOGICAL SOCIETY, San Francisco, April 11-16. Dr. W. F. Hamilton, Medical College of Georgia, Augusta, Ga., Secretary.

AMERICAN PSYCHIATRIC ASSOCIATION, Traymore and Claridge Hotels, Atlantic City, N. J., May 9-13. Dr. William Malamud, 80 East Concord St., Boston 18, Secretary.

AMERICAN PSYCHOSOMATIC SOCIETY, Claridge Hotel, Atlantic City, N. J., May 4-5. Dr. Theodore Lidz, 333 Cedar St., New Haven 11, Conn., Secretary.

AMERICAN RADIUM SOCIETY, Shoreham Hotel, Washington, D. C., April 21-23. Dr. Robert E. Fricke, 102 Second Ave. S.W., Rochester, Minn., Secretary.

AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, Palace Hotel, San Francisco, Apr. 10-15. Dr. Philip Handler, Duke University, Durham, N. C., Secretary.

AMERICAN SOCIETY FOR CLINICAL INVESTIGATION, Haddon Hall, Atlantic City, N. J., May 2. Dr. J. D. Meyers, 622 West 168th St., New York 32, Secretary.

AMERICAN SOCIETY FOR EXPERIMENTAL PATHOLOGY, San Francisco, April 10-16. Dr. Cyrus C. Erickson, 874 Union Avenue, Memphis 3, Tenn., Secretary.

AMERICAN SOCIETY OF MAXILLOFACIAL SURGEONS, Brown Hotel, Louisville, Ky., May 9-11. Dr. John A. Drummond, 1414 Drummond St., Montreal, Canada, Secretary

AMERICAN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, San Francisco, April 10-16. Dr. Carl C. Pfeiffer, Emory University School of Medicine, Emory University, Ga., Secretary.

AMERICAN SURGICAL ASSOCIATION, The Warwick, Philadelphia, April 27-29. Dr. R. Kennedy Gilchrist, 59 East Madison St., Chicago 3, Secretary.

AMERICAN VENEREAL DISEASE ASSOCIATION, Washington, D. C., Apr. 28-29. Dr. John C. Hume, 615 N. Wolfe St., Baltimore 5, Secretary.

ARIZONA MEDICAL ASSOCIATION, El Conquistador, Tucson, May 4-7. Dr. Dermont W. Melick, 401 Security Building, Phoenix, Secretary.

ASSOCIATION OF AMERICAN PHYSICIANS, Chalfonte-Haddon Hall, Atlantic City, N. J., May 3-4. Dr. W. Barry Wood Jr., 600 S. Kingshighway Blvd., St. Louis 10, Secretary.

CALIFORNIA MEDICAL ASSOCIATION, Palace Hotel, San Francisco, May 1-5. Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

CONFERENCE ON MICROCIRCULATORY PHYSIOLOGY AND PATHOLOGY, Benjamin Franklin Hotel, Philadelphia, April 5. Dr. George P. Fulton, Boston University College of Liberal Arts, 725 Commonwealth Ave., Boston 15, Chairman.

CONNECTICUT STATE MEDICAL SOCIETY, Stratfield Hotel, Bridgeport, April 26-28. Dr. Creighton Barker, 160 St. Ronan St., New Haven, Executive Secretary.

EASTERN STATES HEALTH EDUCATION CONFERENCE, New York Academy of Medicine, New York, April 21-22. Dr. Iago Galdston, 2 East 103rd St., New York 29, Secretary.

FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, San Francisco, April 11-15. Dr. M. O. Lee, 2101 Constitution Avenue, Washington, D. C., Secretary.

FLORIDA MEDICAL ASSOCIATION, Vinoy Park Hotel, St. Petersburg, April 3-6. Dr. Samuel M. Day, P. O. Box 1018, Jacksonville, Secretary.

GEORGIA, MEDICAL ASSOCIATION OF, Bon Air Hotel, Augusta, May 1-4. Mr. Milton D. Kreuger, 875 West Peachtree St., Atlanta, Executive Secretary.

HAWAII MEDICAL ASSOCIATION, Honolulu, May 5-8. Dr. Samuel L. Yee, 510 South Beretania St., Honolulu 13, Secretary.

INDUSTRIAL MEDICAL ASSOCIATION, Buffalo, N. Y., April 23-29. Dr. Glenn Gardiner, Inland Steel Co., East Chicago, Ind., Secretary.

INTERNATIONAL ACADEMY OF PROCTOLOGY, Plaza Hotel, New York, March 23-26. Dr. Alfred J. Cantor, 43-55 Kissena Blvd., Flushing, N. Y., Secretary.

IOWA STATE MEDICAL SOCIETY, Veterans' Memorial Auditorium, Des Moines, April 24-27. Dr. R. F. Birge, 529 36th St., Des Moines 12, Secretary.

JOHN A. ANDREW CLINICAL SOCIETY, Memorial Hospital, Tuskegee Institute, Ala., April 3-8. Dr. Eugene H. Dibble Jr., John A. Andrew Memorial Hospital, Tuskegee Institute, Alabama, Secretary.

KANSAS MEDICAL SOCIETY, Baker Hotel, Hutchinson, May 1-5. Dr. J. A. Butin, 315 West Fourth St., Topeka, Secretary.

LOUISIANA STATE MEDICAL SOCIETY, Roosevelt Hotel, New Orleans, May 2-4. Dr. C. Grenes Cole, 1430 Tulane Ave., New Orleans 12, Secretary.

MARYLAND, MEDICAL AND CHIRURGICAL FACULTY OF THE STATE OF, Baltimore, April 21-23. Dr. Everett S. Diggs, 1211 Cathedral St., Baltimore, Secretary.

MID-CENTRAL STATES ORTHOPAEDIC SOCIETY, Sheraton Hotel and St. Louis Medical Society Auditorium, St. Louis, April 15-16. Dr. H. O. Anderson, 3244 East Douglas St., Wichita, Kans., Secretary.

MIDWEST REGIONAL CONFERENCE, AMERICAN PSYCHIATRIC ASSOCIATION, Nebraska Psychiatric Institute, Omaha, Apr. 22-23. Dr. Harold R. Martin, Nebraska Psychiatric Institute, Omaha, Chairman, Program Committee.

MISSISSIPPI STATE MEDICAL ASSOCIATION, Hotel Buena Vista, Biloxi, May 10-12. Mr. Rowland B. Kennedy, 860 Milner Bldg., Jackson, Executive Secretary.

MISSOURI STATE MEDICAL ASSOCIATION, Kansas City, March 27-30. Dr. E. R. Bohrer, 634 North Grand Blvd., St. Louis 3, Secretary.

NATIONAL GASTROINTESTINAL CANCER CONFERENCE, Hosack Hall, New York Academy of Medicine, New York, April 4-5. Dr. Morris K. Barrett, National Cancer Institute, Bethesda 14, Maryland, Executive Secretary.

NEW JERSEY, MEDICAL SOCIETY OF, Ambassador Hotel, Atlantic City, April 17-20. Dr. Marcus H. Greifinger, 315 West State St., Trenton 8, Secretary.

NEW MEXICO MEDICAL SOCIETY, Hilton Hotel, Albuquerque, May 4-6. Mr. Ralph R. Marshall, 223 First National Bank Bldg., Albuquerque, Executive Secretary.

NEW YORK, MEDICAL SOCIETY OF THE STATE OF, Hotel Statler, Buffalo, May 9-13. Dr. Walter P. Anderton, 386 Fourth Avenue, New York 16, Secretary.

NORTH CAROLINA, MEDICAL SOCIETY OF THE STATE OF, Hotel Carolina, Pinehurst, May 2-4. Mr. James T. Barnes, 203 Capitol Club Building, Raleigh, Executive Secretary.

NORTH DAKOTA STATE MEDICAL ASSOCIATION, Hotel Prince, Bismarck, April 30-May 3. Dr. E. H. Boerth, Box 1198, Bismarck, Secretary.

NORTH PACIFIC SOCIETY OF NEUROLOGY AND PSYCHIATRY, Empress Hotel, Victoria, B. C., March 25-26. Dr. John W. Evans, 919 Taylor St. Bldg., Room 805, Portland, Ore., Secretary.

OHIO STATE MEDICAL ASSOCIATION, Netherland-Plaza Hotel, Cincinnati, April 19-21. Mr. Charles S. Nelson, 79 E. State St., Columbus 15, Executive Secretary.

OKLAHOMA STATE MEDICAL ASSOCIATION, Mayo Hotel, Tulsa, May 8-11. Mr. R. H. Graham, 1227 Classen Drive, Oklahoma City, Executive Secretary.

POST GRADUATE INSTITUTE OF THE PHILADELPHIA COUNTY MEDICAL SOCIETY, Bellevue-Stratford Hotel, Philadelphia, March 29-April 1. Dr. Leandro M. Tocantino, 301 South 21st St., Philadelphia 3, Director.

RHODE ISLAND MEDICAL SOCIETY, Rhode Island Medical Society Library, Providence, May 4-5. Dr. Thomas Perry Jr., 106 Francis St., Providence 3, Secretary.

SECTIONAL MEETINGS, AMERICAN COLLEGE OF SURGEONS:

IDAHO, Sun Valley, Sun Valley Lodge, April 18-20. Dr. James H. Hawley, 105 North 8th St., Boise, Chairman.

MANITOBA, Winnipeg, The Fort Garry, April 25-26. Dr. Paul H. T. Thorlakson, Winnipeg Clinic, Winnipeg, Manitoba, Chairman.

TENNESSEE, Nashville, Dinkler-Andrew Jackson Hotel and War Memorial Bldg., April 4-6. Dr. James A. Kirtley Jr., 104 Twentieth Ave. North, Nashville, Chairman.

SOCIETY OF AMERICAN BACTERIOLOGISTS, Statler Hotel, New York, May 8-13. Dr. John Hays Bailey, Sterling Winthrop Research Institute, Rensselaer, N. Y., Secretary.

SOUTH CAROLINA MEDICAL ASSOCIATION, Francis Marion Hotel, Charleston, May 10-12. Dr. Robert Wilson, 165 Rutledge Ave., Charleston, Secretary.

SOUTHEASTERN ALLERGY ASSOCIATION, Orange Court Hotel, Orlando, Fla., March 25-26. Dr. Katharine B. MacInnis, 1515 Bull St., Columbia 1, S. C., Secretary.

SOUTHERN BRANCH, AMERICAN PUBLIC HEALTH ASSOCIATION, New Orleans, May 11-13. Dr. Frank M. Hall, P. O. Box 491, Gainesville, Fla., Secretary.

STUDENT AMERICAN MEDICAL ASSOCIATION, Sherman Hotel, Chicago, May 6-8. Mr. Russell F. Staudacher, 510 N. Dearborn St., Chicago 10, Executive Secretary.

TENNESSEE STATE MEDICAL ASSOCIATION, Read House, Chattanooga, April 10-13. Dr. R. H. Kampmeier, 706 Church St., Nashville 3, Secretary.

TEXAS MEDICAL ASSOCIATION, Texas Hotel, Fort Worth, April 24-27. Dr. J. M. Travis Sr., 1801 North Lamar Blvd., Austin, Secretary.

UNITED STATES-MEXICO BORDER PUBLIC HEALTH ASSOCIATION, Hotel del Bosque, Mexico, D. F., May 6-9. Dr. Sidney B. Clark, 204 U. S. Court, El Paso, Texas, Secretary.

WESTERN BRANCH, AMERICAN PUBLIC HEALTH ASSOCIATION, Phoenix, Ariz., April 19-22. Mrs. L. Amy Darter, Division of Laboratories, State Dept. of Public Health, Berkeley, Calif., Secretary.

WESTERN INDUSTRIAL MEDICAL ASSOCIATION, Sir Francis Drake Hotel, San Francisco, April 30. Dr. Edward J. Zaik, 740 S. Olive St., Room 320, Los Angeles 14, Secretary.

WISCONSIN, STATE MEDICAL SOCIETY OF, Hotel Schroeder, Milwaukee, May 3-5. Mr. Charles H. Crownhart, 704 East Gorham St., Madison 3, Secretary.

FOREIGN AND INTERNATIONAL

ASSOCIATION OF SURGEONS OF GREAT BRITAIN AND IRELAND, University of Glasgow, Glasgow, Scotland, April 14-16. Dr. Henry W. S. Wright, 45 Lincoln's Inn Fields, London W.C.2, England, Hon. Secretary.

AUSTRALASIAN MEDICAL CONGRESS, Sydney, N.S.W., Australia, Aug. 20-27. For information write: Federal Council of the B.M.A. in Australia, 135 Macquaire St., Syndey, N.S.W., Australia.

BRITISH MEDICAL ASSOCIATION, Representative Meeting, London, England, June 1-4. Dr. A. Macrae, B.M.A. House, Tavistock Square, London, W.C.1, England, Secretary.

CANADIAN AND BRITISH MEDICAL ASSOCIATIONS, Joint Meeting, Toronto, Canada, June 20-22. Dr. Arthur D. Kelly, 244 St. George St., Toronto, Canada, General Secretary.

COMMONWEALTH HEALTH AND TUBERCULOSIS CONFERENCE, Royal Festival Hall, London, England, June 21-25. Mr. J. H. Harley Williams, Tavistock House North, Tavistock Square, London, W.C.1, England, Secretary General.

CONGRESS OF INTERNATIONAL ASSOCIATION OF APPLIED PSYCHOLOGY, London, England, July 18-23. Dr. C. B. Frisby, National Institute of Industrial Psychology, 14 Welbeck St., London, W.1, England, President.

CONGRESS OF INTERNATIONAL ASSOCIATION OF PSYCHOTECHNOLOGY, London, England, July 18-23. For information write: Dr. C. B. Frisby, Director, National Institute of Industrial Psychology, 14 Welbeck St., London, W.1, England.

CONGRESS OF THE INTERNATIONAL ASSOCIATION FOR THE STUDY OF THE BRONCHI, Stockholm, Sweden, June 18-19. For information write: Dr. J. M. Lemoine, 187 boulevard St. Germain, Paris 7e, France.

CONGRESS OF INTERNATIONAL DIABETES FEDERATION, Cambridge, England, July 4-8. Mr. James G. L. Jackson, 152 Harley St., London, W.1, England, Executive Secretary General.

CONGRESS OF INTERNATIONAL SOCIETY OF SURGERY, Copenhagen, Denmark, July 23-29. Dr. L. Dejardin, 141 rue Belliard, Brussels, Belgium, General Secretary.

EUROPEAN CONGRESS ON RHEUMATISM, Scheveningen, The Hague, Netherlands, June 13-17. Dr. H. van Swaay, Pieter Bothstraat 12, The Hague, Netherlands, Secretary.

HEALTH CONGRESS OF THE ROYAL SANITARY INSTITUTE, Bournemouth, England, April 26-29. Mr. P. Arthur Wells, Royal Sanitary Institute, 90 Buckingham Palace Road, London, S.W.1, England, Secretary.

HISPANO-PORTUGUESE CONGRESS OF OBSTETRICS AND GYNECOLOGY, Seville, Spain, April 13-16. Dr. M. Recasens, Calle Munoz Olive 7, Seville, Spain, General Secretary.

INTER-AMERICAN CONGRESS OF RADIOLOGY, Shoreham Hotel, Washington, D. C., U. S. A., April 24-29. Dr. Eugene P. Pendergrass, 3400 Spruce St., Philadelphia 4, Pa., U. S. A., Secretary General.

INTERNATIONAL ANATOMICAL CONGRESS, Paris, France, July 25-30. Prof. Gaston Cordier, 45, rue des Saints-Pères, Paris 6e, France, Secretary General.

INTERNATIONAL CONGRESS OF ALLERGOLOGY, Rio de Janeiro, Brazil, S. A., Nov. 6-12. Dr. Bernard N. Halpern, 197 boulevard St. Germain, Paris 7e, France, Secretary General.

INTERNATIONAL CONGRESS OF ANGIOLOGY AND HISTOPATHOLOGY, Fribourg, Switzerland, Sept. 2-5. For information write: Dr. Gerson, 4 rue Pasquier, Paris 8e, France.

INTERNATIONAL CONGRESS OF BIOCHEMISTRY, Brussels, Belgium, Aug. 1-6. Prof. C. Liebecq, 17 Place Delcour, Liège, Belgium, Secretary General.

INTERNATIONAL CONGRESS OF COMPARATIVE PATHOLOGY, Lausanne, Switzerland, May 26-31. Professor Hauduroy, 19 rue Cesar Roux, Lausanne, Switzerland, Secretary General.

INTERNATIONAL CONGRESS OF CRIMINOLOGY, London, England, Sept. 11-18. For information write: Dr. Carroll, 28 Weymouth St., London, W.1, England.

INTERNATIONAL CONGRESS OF EUROPEAN SOCIETY OF HAEMATOLOGY, Freiburg i,Br., Germany, Sept. 20-24. Prof. Dr. L. Heilmeyer, Hugstetter Strasse 55, Freiburg i,Br., Germany, Chairman.

INTERNATIONAL CONGRESS OF LIBRARIANSHIP AND DOCUMENTATION, Brussels, Belgium, Sept. 11-18. For information write: Dr. A. C. Breycha-Vauthier, Librarian, United Nations, Geneva, Switzerland.

INTERNATIONAL CONGRESS OF NEUROPATHOLOGY, London, England, Sept. 12-17. Dr. W. H. McMenemey, Maida Vale Hospital for Nervous Diseases, London, W.9, England, Secretary.

INTERNATIONAL CONGRESS OF PLASTIC SURGERY, Stockholm, Sweden, Aug. 1-4, and Uppsala, Sweden, Aug. 5. Dr. Tord Skoog, Uppsala, Sweden, General Secretary.

INTERNATIONAL CONGRESS ON URINARY LITHIASIS, Evian, France, Sept. 2-4. Mr. Rossollin-Grandville, Direction Cachet, Evian (Hte-Savoie), France, Secretary General.

INTERNATIONAL CONGRESS OF UROLOGY, Athens, Greece, April 10-18. Dr. Z. Kaires, 25, rue Voukourestion, Athens, Greece, Secretary General.

INTERNATIONAL HOSPITAL CONGRESS, Lucerne, Switzerland, May 29-June 3. Capt. J. E. Stone, International Hospital Federation, 10 Old Jewry, London, E.C.2, England, Hon. Secretary.

INTERNATIONAL MEDICAL CONGRESS, Verona, Italy, Sept. 1-4. For information write: c/o Offices of the International Verona Fair, Piazza Bra., Verona, Italy.

INTERNATIONAL SOCIETY FOR THE STUDY OF BIOLOGICAL RHYTHMS, Stockholm, Sweden, Sept. 15-17. For information write: Prof. Ture Petrén, Karolinska Institutet, Stockholm 60, Sweden.

INTERNATIONAL SURGICAL CONGRESS, Geneva, Switzerland, May 23-26. Dr. Max Thorek, 1516 Lake Shore Drive, Chicago, Illinois, U. S. A., Secretary General.

INTERNATIONAL SYNDICATE OF GYNECOLOGISTS AND OBSTETRICIANS, Meeting Hall of Medical Societies, Paris, France, June 27-28. Dr. Jacques Courtois, 1, rue Racine, Saint-Germain-en-Laye (S & O), France, Secretary General.

INTERNATIONAL UNION OF GYNECOLOGISTS AND OBSTETRICIANS, Paris, France, June 27-28. For information write: Dr. J. Courtois, 1, rue Racine, Saint-German-en-Laye, France.

IRISH OPHTHALMOLOGICAL SOCIETY, Dublin, Ireland, May 12-14. For information write: Dr. W. L. Benedict, 100 First Ave. Bldg., Rochester, Minnesota, U. S. A.

JAPAN MEDICAL CONGRESS, Kyoto University and Kyoto Prefectural Medical College, Kyoto, Japan, April 1-5. Dr. Mitsuharu Goto, University Hospital, Medical Faculty of Kyoto University, Kyoto, Japan, Secretary General.

LATIN AMERICAN ELECTROENCEPHALOGRAPHICAL CONGRESS, Montevideo, Uruguay, S. A., March 21-24. For information write: Dr. R. Arana-Iniquez, Convencion 1287, Montevideo, Uruguay, S. A.

LATIN AMERICAN NEUROSURGICAL CONGRESS, Montevideo, Uruguay, S. A., March 21-24. For information write: Dr. R. Arana-Iniquez, Convencion 1287, Montevideo, Uruguay, S. A.

MIDDLE EAST MEDICAL ASSEMBLY, Campus of American University of Beirut, Beirut, Lebanon, April 22-24. Dr. John L. Wilson, American University of Beirut, Beirut, Lebanon, Chairman.

NEURORADIOLOGIC SYMPOSIUM, London, England, Sept. 13-17. Dr. R. D. Hoare, National Hospital, Queen Square, London, W.C.1, England, Secretary.

PAN AMERICAN CONGRESS OF OPHTHALMOLOGY, Santiago, Chile, S. A., Jan. 9-14, 1956. Dr. Rene Contardo, Huerfanos 930, Of. 74, Santiago, Chile, Secretary General.

PAN AMERICAN CONGRESS ON RHEUMATIC DISEASES, Rio de Janeiro and Sao Paulo, Brazil, S. A., Aug. 14-20. For information write: Dr. Waldemar Bianchi, 126 Avenida Franklin D. Roosevelt, Rio de Janeiro, Brazil, S. A.

VENEZUELAN CONGRESS OF MEDICAL SCIENCES, Caracas, Venezuela, S. A., Nov. 18-26. Dr. A. L. Briceno Rossi, Apartado 4412, Ofic. del Este, Caracas, Venezuela, S. A., Secretary General.

WORLD CONGRESS OF ANESTHESIOLOGISTS, Scheveningen, Netherlands, Sept. 5-10. For information write: Mr. W. A. Fentener van Vlissingen, Noord-Houdringelaan, 24, Bilthoven, Netherlands.

WORLD FEDERATION FOR MENTAL HEALTH, Istanbul, Turkey, Aug. 21. For information write: Miss E. M. Thornton, 19 Manchester St., London, W.1, England.

WORLD MEDICAL ASSOCIATION, Vienna, Austria, Sept. 20-26. Dr. Louis H. Bauer, 345 East 46th St., New York 17, N. Y., U. S. A., Secretary General.

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 21-23. Sec., Dr. D. G. Gill, 537 Dexter Ave., Montgomery 4.

ARIZONA:* *Examination and Reciprocity.* Phoenix, April 13-15. Ex. Sec., Mr. Robert Carpenter, 401 Security Bldg., Phoenix.

ARKANSAS:* *Examination.* Little Rock, June 9-10. Sec., Dr. Joe Verser, Harrisburg.

CALIFORNIA: *Written.* San Francisco, June 20-23; Los Angeles, Aug. 22-25; and Sacramento, Oct. 17-20. *Oral and Clinical Examinations for Foreign Medical School Graduates.* San Francisco, June 19; Los Angeles, Aug. 21; and San Francisco, Nov. 13. *Oral Examination for Reciprocity Applications.* San Francisco, June 18; Los Angeles, Aug. 20; and San Francisco, Nov. 12. Sec., Dr. Louis E. Jones, Room 536, 1020 N Street, Sacramento.

COLORADO:* *Examination.* Denver, June 14-15. Final date for filing applications is May 13. *Reciprocity.* Denver, April 12. Final date for filing applications was March 14. Exec. Sec., Miss Beulah H. Hudgens, 831 Republic Bldg., Denver 2.

DELAWARE: *Examination.* Dover, July 12-14. *Endorsement.* Dover, July 21. Final date for filing applications is June 15. Sec., Dr. Joseph S. McDaniel, Dover.

DISTRICT OF COLUMBIA:* *Examination.* Washington, May 9-10. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Avenue, N.W., Washington.

FLORIDA:* *Examination.* Jacksonville, June 26-28. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami.

GEORIGA: *Examination.* Atlanta and Augusta, June 7-8. *Reciprocity.* June 9. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta.

INDIANA: *Examination.* Indianapolis, June 21-23. Exec. Sec., Miss Ruth V. Kirk, 538 K. of P. Building, Indianapolis.

IOWA:* *Examination.* Iowa City, June 13-15. Exec. Sec., Mr. Ronald V. Saf, State Office Bldg., Des Moines.

KANSAS: *Examination and Endorsement.* Kansas City, June 8-9. Sec., Dr. O. M. Davidson, 872 New Brotherhood Bldg., Kansas City.

KENTUCKY: *Examination.* Louisville, June 6-8. Asst. Sec., Mr. Raymond F. Dixon, 620 S. 3rd St., Louisville.

LOUISIANA: *Homeopathic. Examination and Reciprocity.* Subject to Call. Sec., Dr. F. H. Hardenstein, 903 Pere Marquette Bldg., New Orleans 12.

MARYLAND: *Regular Examination.* Baltimore, June 21-24. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore 18. *Homeopathic. Reciprocity.* Washington, D. C., April 12. *Examination. Written.* Baltimore, June 20-22. Sec., Dr. Robert H. Reddick, Eastern Shore State Hospital, Cambridge.

MASSACHUSETTS: *Examination.* Boston, July 12-15. Sec., Dr. Robert C. Cochrane, Room 37, State House, Boston.

MICHIGAN:* *Examination.* Ann Arbor and Detroit, June 15-17 (tentative). Sec., Dr. J. Earl McIntyre, 118 Stevens T. Mason Bldg., Lansing 8.

MINNESOTA:* *Examination.* Minneapolis, April 19-21 and June 14-16. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSISSIPPI: *Examination and Reciprocity.* Jackson, June 27-29. Asst. Sec., Dr. R. N. Whitfield, State Board of Health, Jackson.

MONTANA: *Examination and Reciprocity.* Helena, April 4-6. Sec., Dr. S. A. Cooney, 214 Power Block, Helena.

NEBRASKA:* *Examination.* Omaha, June. Director, Bureau of Examining Boards, Mr. Husted K. Watson, State Capitol Bldg., Room 1009, Lincoln 9.

NEVADA:* *Examination and Reciprocity.* Reno, April 5. Sec., Dr. G. H. Ross, 112 N. Curry St., Carson City.

NEW MEXICO:* *Examination and Reciprocity.* Santa Fe, Apr. 11-12. Sec., Dr. R. C. Derbyshire, 227 E. Palace Ave., Santa Fe.

NORTH CAROLINA: *Examination.* Raleigh, June 20-23. *Reciprocity.* Pinehurst, May 2. Sec., Dr. Joseph J. Combs, 716 Professional Building, Raleigh.

NORTH DAKOTA: *Examination.* Grand Forks, July 6-8. *Reciprocity.* Grand Forks, July 9. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Reciprocity.* Columbus, April 5. *Written.* Columbus, June 13-15. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

OKLAHOMA:* *Examination.* Oklahoma City, June 7-8. Sec., Dr. C. Gallagher, 813 Braniff Bldg., Oklahoma City.

OREGON:* *Examination.* Portland, July. *Reciprocity.* Portland, April 7-9. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland 4.

PENNSYLVANIA: *Examination.* Philadelphia and Pittsburgh, July. Acting Sec., Mrs. Marguerite G. Steiner, Box 911, Harrisburg.

RHODE ISLAND:* *Examination.* Providence, April 7-8. Administrator of Professional Regulation, Mr. Thomas B. Casey, Room 366, State Office Bldg., Providence.

SOUTH CAROLINA: *Examination and Reciprocity.* Columbia, June 27-29. Sec., Mr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA:* *Examination and Reciprocity.* Rapid City, July 19-20. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

TENNESSEE:* *Examination.* Memphis, March 30-31. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis.

TEXAS:* *Examination and Reciprocity.* Fort Worth, June 20-22. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

VIRGINIA: *Examination.* Richmond, June 16-18. *Reciprocity.* Richmond, June 15. Address: The Secretary, 631 First St., S.W., Roanoke.

WASHINGTON:* *Examination and Reciprocity.* Seattle, July 10-13. Sec., Mr. Edward C. Dohm, Capitol Bldg., Olympia.

WEST VIRGINIA: *Reciprocity.* Charleston, April 4. Sec., Dr. N. H. Dyer, State Office Bldg., No. 3, Charleston 5.

WISCONSIN:* *Reciprocity.* Madison, April 14-16. The board will also interview applicants for Temporary Educational Permits who have commenced their training previous to the meeting. Sec., Dr. Thomas W. Tormey, Room 1140, State Office Bldg., Madison 2.

WYOMING: *Examination and Reciprocity.* Cheyenne, June 6. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

ALASKA:* On application. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Sec., Dr. John E. Kennedy, Agana.

HAWAII: *Examination.* Honolulu, July 11-14. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

VIRGIN ISLANDS: *Examination and Reciprocity.* St. Thomas, June 8-9. Sec., Dr. Earle M. Rice, St. Thomas.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: *Reciprocity.* Phoenix, April 16. Sec., Dr. M. R. Richter, 2910 N. 7th Ave., Phoenix.

ARKANSAS: *Examination.* Little Rock, May 3-4. Sec., Mr. S. C. Dellinger, Zoology Dept., University of Arkansas, Fayetteville.

DISTRICT OF COLUMBIA: *Examination.* Washington, April 18-19. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., N.W., Washington.

FLORIDA: *Examination.* Miami and Gainesville, May 14. Sec., Mr. M. W. Emmel, Box 340, University of Florida, Gainesville.

IOWA: *Examination.* Des Moines, April 12. Sec., Dr. Ben H. Peterson, Coe College, Cedar Rapids.

MINNESOTA: *Examination.* Minneapolis, April 5-6. Sec., Dr. Raymond N. Bieter, 126 Millard Hall, University of Minnesota, Minneapolis.

NEBRASKA: *Examination.* Omaha, May 3-4. Director, Mr. Husted K. Watson, 1009 State Capitol, Lincoln.

NEVADA: *Examination.* Reno, April 5. Sec., Dr. Donald G. Cooney, Box 9002, University Station, Reno.

OKLAHOMA: Oklahoma City, April 7-8. Sec., Dr. C. Gallagher, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, June 4, Sept. 10, and Dec. 3. Sec., Mr. Charles D. Byrne, State Board of Higher Education, Eugene.

SOUTH DAKOTA: *Examination.* Vermillion, June 10-11. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.

TEXAS: *Examination.* Galveston, Houston and Dallas, April 15-16. Chief Clerk, Mrs. Betty Ratcliff, 407 Perry-Brooks Bldg., Austin.

WASHINGTON: *Examination.* Seattle, July 6-7. Sec., Mr. Edward C. Dohm, Capitol Bldg., Olympia.

WISCONSIN: *Examination.* Milwaukee, May 14. Sec., Mr. William H. Barger, 621 Ransom St., Ripon.

ALASKA: On application. Juneau or other towns in Territory as decided by Board. *Reciprocity.* On application. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

*Basic Science Certificate required.

MAGAZINE–TELEVISION REPORT

The following list of current medical articles in mass-circulation magazines and forthcoming network television programs on medical subjects is published each week only for the information of readers of THE JOURNAL. *Unless specifically stated, the American Medical Association neither approves nor disapproves of the articles and programs reported.*

TELEVISION

Monday, March 21, 1955

NBC-TV, 9 p. m. EST. "Medic." Titled "Death Is a Red Balloon," the story tells of a congenital brain aneurysm and the choice a patient has to make between taking her chances of a sudden death or undergoing brain surgery to clamp the artery.

MAGAZINES

McCall's, April, 1955

"The Doctor's Wife Talks Back," by Harriet Newton

In answer to charges of high fees, long reception room waits, and other complaints, a doctor's wife tells of the long years of schooling, the high overhead of medical practice, the fatiguing 'round-the-clock demands made on her husband, and the sacrifice of normal family home life that the physician makes to care for his patients.

Seventeen, March, 1955

"A Doctor Fills You in on the Facts," by Joseph D. Wassersug, M.D.

"Menstruation is not a 'sick time,' but a normal, rather wonderful process which is the first sign of a young girl's development toward maturity and womanhood." A physiological explanation of menstruation as a normal body function, written to dispel fear and erroneous beliefs.

Collier's, March 18, 1955

"Tattoos for Everyone," by Ann Cutler

The Federal Civil Defense Committee has developed a plan to tattoo on each American his blood type for ready identification in time of disaster.

Good Housekeeping, April, 1955

"How to Live to Be 100," by Maxine Davis

This article explains that it is disease, not old age, that kills elderly people; as medical science advances in the field of geriatrics, life expectancy increases. A survey of centenarians revealed that a person's activities and attitudes were also vital to his longevity. Among findings were that the majority of centenarians were independent, self-reliant, gregarious, and active in useful work.

The American Weekly, March 13, 1955

"My Lonely Struggle with Morphine," by Richard Barnitz

The author tells how he became addicted to morphine while easing the pain caused by several sympathectomies. Because he did not wish to go to a federal hospital, he sought treatment from his family doctor. In the following two month ordeal of breaking the addiction, his physician prescribed decreasing amounts of morphine, codeine, strychnine, and finally placebos. The patient describes the intense craving that he forced himself to overcome.

The American Weekly, March 20, 1955

"Five Steps to Good Feet," by William M. Scholl, M.D.

This brief article sets up a five-point program for foot care: 1. Learn about your feet. 2. Buy only the shoes that fit. 3. Buy stockings that fit. 4. Give your feet reasonable care. 5. Don't wear the same pair of shoes on successive days. The writer urges consultation with a chiropodist or orthopedist when foot ailments occur.

"A Sister for Barbie," by Mrs. Sheila Erdman

After two years of treatment for poliomyelitis that left her paralyzed from the hips down, the writer and her husband decided to have another child, despite her disability. The baby was born and brought joy to the mother, who again considered herself a vital, productive human being.

Parade, March 13, 1955

"Found: New Relief for Arthritis," by Robert P. Goldman

An optimistic article that relates the improvement of rheumatoid arthritic patients when treated with Meticorten and Meticortelone, "the best thing we've seen since cortisone." The writer warns, however, that researchers at the National Arthritis Institute have not yet determined whether the drug will produce dangerous side-effects, and quotes a doctor: "We have made a big advance—you can see that in our patients—but we've still got a way to go."

Better Living, April, 1955

"16 Straight Answers on Good Food—Good Health," by Dr. Herbert Pollack

A physician answers questions on proper nutrition, symptoms of nutritional deficiency, essential calories and foods, cooking methods, anemia, excessive weight, and weight reduction.

Look, March 22, 1955

"Wheel-Chair Doctor," by Joseph Morschauser and Bob Sandberg

A picture layout on how a young physician practices medicine despite his confinement to a wheel chair. He is crippled as a result of poliomyelitis suffered in 1953 when he was a medical student.

DEATHS

Menville, Leon J. ✠ New Orleans; born in Napoleonville, La., Nov. 27, 1882; Maryland Medical College, Baltimore, 1904; specialist certified by the American Board of Radiology; joined the faculty of Tulane University of Louisiana School of Medicine in 1919 and later became professor of radiology, serving until his retirement in 1948 with the title of professor emeritus; member of the House of Delegates of the American Medical Association in 1941, 1942, 1943, and 1945; past president of the Louisiana State Medical Society and the Radiological Society of North America, which in 1932 awarded him its gold medal for original work on the lymphatic system and in 1953 elected him to honorary life membership; in 1934 was presented with the annual award of the Louisiana Academy of Science; member and past vice-president and chancellor of the American College of Radiology; member of the American Roentgen Ray Society, Society for Experimental Biology and Medicine, Southern Medical Association, Louisiana State Radiological Society, and the American Radium Society; represented the United States as a delegate to the International Congress of Radiology in Buenos Aires, and later was a delegate to the congress at its meeting in Cuba; honorary member of the Radiological Society of Cuba and a corresponding member of the National Academy of Medicine of the Republic of Columbia; past president of the Louisiana State Board of Medical Examiners; served during World War I; during World War II was a member of the selective service board and held a commission in the Naval Reserve; for many years director of the radiology department at Charity Hospital; radiologist at the French and Illinois Central hospitals and consultant at Hotel Dieu and Flint-Goodridge hospitals in New Orleans; served on the editorial board of the *American Journal of Cancer* and as a committee member of the *New Orleans Medical and Surgical Journal;* for many years editor of *Radiology;* contributing author to "Pohle's Clinical Radiation Therapy," "Pillmore's Clinical Radiology," and "Medical Clinics of North America"; died Jan. 24, aged 72.

Davis, David John ✠ Chicago; born in Racine, Wis., Aug. 9, 1875; Rush Medical College, Chicago, 1903; received the degree of Ph.D. from the University of Chicago; in 1910 studied abroad in Vienna and Freiburg; on his return he was pathologist at St. Luke's Hospital; on a part-time basis was assistant professor of pathology at his alma mater from 1909 to 1913, when he became chairman of the department of pathology and bacteriology at the University of Illinois College of Medicine, where in 1924 he became dean; held both of these positions until his retirement on Sept. 1, 1943, with the title of dean and professor of pathology emeritus; the university established the D. J. Davis Lectureship on Medical History in his honor; member of the House of Delegates of the American Medical Association, 1922-1924, 1927-1930, 1933 and 1936; past president of the Institute of Medicine of Chicago; fellow of the American College of Physicians; permanent historian of the Illinois State Medical Society; formerly chairman of the Municipal Tuberculosis Sanitarium and past president of the board; died Dec. 19, 1954, aged 79, of coronary occlusion.

Schlesinger, Monroe Jacob, Boston; born in New York City June 21, 1892; Harvard Medical School, Boston, 1926; professor of pathology, and from 1952 to 1954 clinical professor of pathology at his alma mater, where he served on the faculty in various capacities for many years; certified by the National Board of Medical Examiners; specialist certified by the American Board of Pathology; past president of the New England Pathological Society; member of the American Association of Pathologists and Bacteriologists, College of American Pathologists, American Society for Experimental Pathology, and the Society of American Bacteriologists; a member and councilor of the Massachusetts Medical Society; for many years consulting pathologist at the Jewish Memorial Hospital; consulting pathologist and at one time pathologist-in-chief at the Beth Israel Hospital, where he was recently honored by his staff and associates when a lecture was established in his name; died in the Beth Israel Hospital Jan. 20, aged 62, of acute myocardial infarct.

Agnew, William John Clarke ✠ Rear Admiral, U. S. Navy, retired, Coronado, Calif.; born in High Falls, N. Y., Dec. 6, 1891; University of Vermont College of Medicine, Burlington, 1914; interned at St. John's Riverside Hospital in Yonkers, N. Y.; entered the U. S. Navy in 1917; served during World War I; deputy chief of the Bureau of Medicine and Surgery during World War II; was awarded the Legion of Merit; promoted to rear admiral in 1942; at the time of his retirement in May, 1952, was commanding officer of the National Naval Medical Center at Bethesda, Md.; served as district medical officer of the 11th, 14th, and 9th Naval districts; fellow of the American College of Surgeons; member of the Alpha Kappa Kappa and Theta Nu Epsilon fraternities; died in the Naval Hospital, San Diego, Jan. 25, aged 63, of cerebral thrombosis.

Bogart, Donald Weeks, New York City; born in Warren, Pa., Aug. 16, 1905; Cornell University Medical College, New York, 1933; interned at the Lenox Hill Hospital; formerly resident at the New York Eye and Ear Infirmary, where he was later on the staff; certified by the National Board of Medical Examiners; specialist certified by the American Board of Ophthalmology; for many years on the faculty of the New York University College of Medicine; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; on the staff of the Bellevue Hospital; died Jan. 28, aged 49, of coronary arteriosclerosis.

Wilson, Stanley Albert ✠ Salem, Mass.; born in Brattleboro, Vt., March 19, 1897; University of Vermont College of Medicine, Burlington, 1920; specialist certified by the American Board of Radiology; member of the American Roentgen Ray Society, New England Roentgen Ray Society, and the American College of Radiology; consultant in roentgenology at Essex County Tuberculosis Hospital in Middleton, Mary A. Alley Hospital in Marblehead, Addison Gilbert Hospital in Gloucester, and Cable Memorial Hospital in Ipswich; since 1937 roentgenologist at the Salem Hospital, where he died Jan. 11, aged 57, of heart disease.

Cousar, John Bradley ✠ Columbia, S. C.; born in Bishopville Feb. 21, 1905; University of Virginia Department of Medicine, Charlottesville, 1931; while in Bishopville was president of the Lee County Medical Society; served with distinction with the Armed Forces during World War II, both in the United States and in Europe; received the Purple Heart and the Cross of Honor during his service in Europe; assistant chief medical officer with the Veterans Administration Regional Office; died in the Veterans Administration Hospital Oct. 21, 1954, aged 49, of myocardial infarction and recurrent coronary thrombosis.

Allen, Ellery George ✠ Syracuse, N. Y.; born in Clyde, N. Y., Dec. 4, 1900; Harvard Medical School, Boston, 1926; certified by the National Board of Medical Examiners; fellow of the American College of Physicians; clinical professor of medicine at State University of New York College of Medicine at Syracuse; during the early part of World War II, served as a major with the Army Medical Corps; attending physician and attending hematologist, St. Joseph's Hospital; attending physician, University Hospital; associate in clinical pathology at Syracuse Memorial Hospital; died Jan. 4, aged 54.

Adams, Iduma Ormond, Farina, Ill.; Louisville (Ky.) Medical College, 1898; died Jan. 19, aged 87, of cancer.

Adams, Marvin Edward, Duluth, Minn.; University of Minnesota Medical School, Minneapolis, 1935; served during World War II; died in St. Luke's Hospital Dec. 11, 1954, aged 51.

✠ Indicates Member of the American Medical Association.

Adcock, David Filmore ✠ Columbia, S. C.; Medical College of Virginia, Richmond, 1928; in 1954 president of the Columbia Medical Society; fellow of the American College of Surgeons; on the staffs of the Columbia, Providence, and Good Samaritan-Waverly hospitals; interned and was secretary of the staff at the South Carolina Baptist Hospital; died Jan. 3, aged 52.

Ale, William T., Detroit; Wayne University College of Medicine, Detroit, 1932; served during World War II; died Jan. 24, aged 50, of coronary occlusion.

Alexander, James Minor ✠ Abilene, Texas; Louisville (Ky.) Medical College, 1889; on the staff of the Hendrick Memorial Hospital, where he was at one time chief-of-staff; died Nov. 10, 1954, aged 87, of coronary occlusion.

Baker, George Erwin ✠ Casper, Wyo.; University of Nebraska College of Medicine, Omaha, 1931; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; past president and secretary of the Wyoming State Medical Society; past president of the Natrona County Medical Society; served as county health officer; on the staff of the Natrona County Memorial Hospital, where he died Dec. 18, 1954, aged 49, of coronary occlusion.

Baker, Gerdon Edward ✠ Forty Fort, Pa.; Medico-Chirurgical College of Philadelphia, 1915; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; associated with the Wilkes-Barre (Pa.) General Hospital; member of the board of health and a director of the Forty Fort State Bank; died Jan. 10, aged 75, of coronary thrombosis.

Balcom, Kenneth Ira ✠ Worcester, Mass.; Harvard Medical School, Boston, 1910; died Jan. 2, aged 71, of Hodgkin's disease.

Balla, Morris ✠ South Bend, Ind.; Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest, Hungary, 1915; county health officer; on the staffs of the Memorial and St. Joseph's hospitals; died Dec. 18, 1954, aged 63, of cancer of the lung.

Bender, William Ralph, Hagerstown, Md.; University of the South Medical Department, Sewanee, Tenn., 1908; also a graduate in pharmacy; on the staff of the Washington County Hospital, where he died Dec. 29, 1954, aged 67, of arteriosclerotic heart disease.

Bergquist, Karl Emil ✠ Battle Lake, Minn.; Minneapolis College of Physicians and Surgeons, 1897; member of the American Trudeau Society; served as medical superintendent of the Otter Tail County Sanatorium; died in Fergus Falls Dec. 10, 1954, aged 80.

Campbell, Robert Wilson, Cass Lake, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1905; died in the Methodist Hospital, Rochester, Dec. 13, 1954, aged 75, of carcinoma of the bladder.

Canby, Joseph Edward ✠ West Hartford, Conn.; Jefferson Medical College of Philadelphia, 1927; member of the Industrial Medical Association; died in Hartford (Conn.) Hospital Jan. 2, aged 54, of myocardial infarction.

Cleveland, Harold Frank ✠ Springfield, Mass.; Middlesex College of Medicine and Surgery, Cambridge, 1920; died in the Springfield Hospital Jan. 19, aged 65, of pyelonephritis with uremia and diabetes mellitus.

Cody, Burtis Lysander, Evansville, Ind.; St. Louis University School of Medicine, 1903; member of the Indiana State Medical Association; served on the board of health; veteran of World War I; died Jan. 10, aged 72, of carcinoma of the lung.

Crum, Harry Herbert, Ithaca, N. Y.; Cleveland Homeopathic Medical College, 1900; first honorary president of the Tompkins County Tuberculosis and Public Health Association; for many years physician of the Tompkins County Jail; at one time city health officer; died in Key West, Fla., Jan. 2, aged 83, of cerebral anoxia and congestive heart failure.

Davis, George, Columbus, Ohio; Medical College of Ohio, Cincinnati, 1900; while practicing in Xenia, served as vice-president of the Greene County Medical Society; veteran of the Spanish-American War; died Dec. 4, 1954, aged 82.

Herold, Herman Cleveland Herbert, Montclair, N. J.; University and Bellevue Hospital Medical College, New York, 1911; for many years chief of obstetrical service, Newark City Hospital; died in the Mountainside Hospital, Glen Ridge, Jan. 14, aged 68, of myocardial infarction and diabetes mellitus.

Mershimer, William Clayton ✠ Junction, Ill.; Rush Medical College, Chicago, 1896; died Jan. 28, aged 87, of myocarditis.

Meserve, John Shackford, Los Angeles; Dartmouth Medical School, Hanover, N. H., 1900; died Jan. 19, aged 81, of bronchopneumonia.

Powers, Jerome ✠ Hohenwald, Tenn.; Vanderbilt University School of Medicine, Nashville, 1921; died in the Vanderbilt University Hospital, Nashville, Dec. 30, 1954, aged 58.

Pusch, Jerome Bernard ✠ Chicago; Chicago College of Medicine and Surgery, 1917; died in the Hospital of St. Anthony de Padua Jan. 22, aged 69, of multiple myeloma.

Robinson, Henry W. ✠ Livingston, Ala.; Memphis (Tenn.) Hospital Medical College, 1901; died Jan. 10, aged 81, of myocardial decompensation.

Romine, John Henry ✠ Webster City, Iowa; Creighton University School of Medicine, Omaha, 1935; past president of the Hamilton County Medical Association; on the staff of the Hamilton County Public Hospital, where he died Jan. 17, aged 43, of cerebral vascular accident.

Rusk, John Alexander, Tremont, Ill.; Barnes Medical College, St. Louis, 1897 and 1898; killed Feb. 9, aged 80, when struck by a passenger train.

Sterbini, Dominico A. ✠ Colfax, Ill.; Regia Universita degli Studi di Roma. Facolta di Medicina e Chirurfia, Italy, 1920; served with the Italian army during World War I; died Jan. 23, aged 61, of coronary disease.

Sterner, Ernest G. ✠ St. Paul; Minneapolis College of Physicians and Surgeons, medical department of Hamline University, 1906; past president of the Ramsey County Medical Society; on the staff of the Bethesda Hospital, where he was past chief of staff and where he died Jan. 20, aged 72, of arteriosclerotic cardiovascular disease.

Talmage, Carl Hubert ✠ Glendale, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1930; assistant clinical professor of surgery at his alma mater; certified by the National Board of Medical Examiners; formerly on the staff of St. Helena Sanitarium and Hospital in Sanitarium; died Jan. 16, aged 52.

Townsend, Louis Jefferson ✠ Belle Fourche, S. D.; Rush Medical College, Chicago, 1896; associated with the John Burns Memorial Hospital, where he died Jan. 17, aged 84, of chronic myocarditis.

Truitt, James Joshua ✠ Houston, Texas; University of Texas School of Medicine, Galveston, 1925; clinical associate professor of medicine at Baylor University College of Medicine; on the staffs of St. Joseph's Infirmary and Hermann Hospital; died Jan. 18, aged 59, of a heart attack.

Vunk, Raymond Hudson ✠ Memphis, Tenn.; Medical College of the State of South Carolina, Charleston, 1935; specialist certified by the American Board of Obstetrics and Gynecology; served in the South Pacific during World War II; on the staffs of the John Gaston Hospital and Methodist Hospital, where he died Jan. 17, aged 46, of coronary thrombosis.

Wagner, Jerome ✠ New York City; Cornell University Medical College, New York, 1907; clinical professor of proctology at New York Polyclinic Medical School and Hospital; fellow of the International College of Surgeons; served in France during World War I; died in Stamford (Conn.) Hospital Feb. 3, aged 68, of acute myocardial infarction and coronary occlusion.

Willson, Jesse O'Neal ✠ Spartanburg, S. C.; Medical College of the State of South Carolina, Charleston, 1912; on the staff of the Spartanburg General Hospital, where he died Jan. 16, aged 65, of coronary thrombosis and benign hypertrophy of the prostate.

FOREIGN LETTERS

BELGIUM

Physicians' National Service.—The newly created Physicians' National Service is a nonprofit organization that provides medical care at low cost to persons of modest means, whether or not they are insured. The physicians themselves decided to organize this service after an attempt on the part of the government to nationalize medicine. So far 4,000 out of the 7,000 practicing physicians in Belgium have pledged their support to the service, and 2,400 contracts have already been validated. These contracts stipulate that the physicians who have signed them must charge persons of modest income the prices established by the ministerial committee of the National Funds for Sickness-Disability Insurance. These prices are slightly higher than the reimbursement rates of the mutual insurance companies. The physicians agree with the National Funds Committee that the patients should pay some of their expenses. This goes far in preventing the abuse of the services of the physicians. The participating physicians will also give special consideration to all persons, insured or not, whose family income does not exceed 100,000 francs plus 8,000 francs for each person in the household who is independent of the head of the household. The physician must also apply this rule to any miner, regardless of income. An innovation of the Physicians' National Service will be a bureau for the settlement of costly fees. This bureau will enable the impecunious person to secure the services of the surgeon of his choice instead of having to accept those of whatever surgeon is attached to the insurance company, as at present. Thus, the Physicians' National Service will respect the liberty of the patient and that of the physician, which respect is essential in order to avoid the advent of a system of medicine with discounts for the poor. With the realization of this plan the physicians are not responding with philosophic protestations but are taking the initiative in measures to make medical treatment more accessible to large groups within the population.

Surgical Treatment of Gastric Cancer.—In the *Acta medica belgica,* Deloyers and Moyson reported a series of 150 patients with gastric cancer treated surgically and formulated guiding principles for bettering the long-term results of gastrectomy for this disease. Any person over 40 years of age, who has gastric distress, must be suspected of having a neoplasm. Those with the greatest risk are the patients with ulcers whose pain is alleviated by eating. The niche may even disappear from the roentgenogram because of filling by the neoplasm. In these patients normochlorhydria or hyperchlorhydria may exist, which makes titration of the gastric contents of little diagnostic value. The authors concluded that all gastric polyps metastasize in time and should be resected. Using strict histological criteria, they calculated that malignant degeneration occurred in at least 10% of patients with gastric ulcer and that any gastric lesion appearing after the age of 40 should be surgically removed.

Gastroscopy and Gastritis.—At a meeting of the Belgian Society of Gastroenterology, Moutier and Cornet reported a series of 1,761 patients with gastritis. The classification decided on by the authors takes into account the gross and microscopic findings. The authors found gastritis in 1,131 men and 630 women in about 15,000 gastroscopies. They divided the stomach into four zones: the upper zone, which is almost impossible to see with a gastroscope and is therefore called the "silent" zone; the middle zone or zone of tolerance, which is easy to examine; the central zone or zone of reaction, which is also easily examined; and the pyloric zone or zone of intolerance, which is difficult to see. Gastroscopy enables the diagnostician to interpret the results given by radiography and chemical studies.

The items in these letters are contributed by regular correspondents in the various foreign countries.

BRAZIL

Fight Against Cancer.—The Brazilian press recently announced that the Service of Medical Fiscalization prohibited the sale of cancer remedies having a secret composition. Supposedly miraculous cancer cures prepared and sold by charlatans have recently received much sensational publicity despite the fact that their sale is illegal. Such a state of affairs acts as a hindrance to the official and scientific fight against cancer. In 1952 there were over 50,000 deaths from cancer in Brazil. The National Cancer Service was created by the government in 1941. In 1954 the federal government distributed 100 million cruzeiros to various organizations engaged in fighting cancer. The Radium Institute, affiliated with the São Paulo University, has participated in the fight against cancer since 1920. It has 80 beds and treats about 2,500 patients a year. Its staff consists of 18 specialists, and it has 1,350 mg. of radium. The Association for the Fight Against Cancer of São Paulo, organized in 1934, operates a 310 bed hospital, the Instituto Central, with a staff of 57 physicians including 35 residents. The average daily work load in this hospital includes 130 new consultations, 150 applications for radiotherapy, and 15 surgical operations. This institute has 11,500 mg. of radium.

The result of educational campaigns was that the index of inoperability, which in the state of São Paulo in 1947 was 54%, had dropped by 1951 to 19%. This was due to the efforts of 39 committees in different cities. Early in 1954, 19 similar campaigns were organized in other Brazilian states. About 450 newspapers and 300 radio stations cooperated in this campaign. The Institute of National Cancer Service in Rio de Janeiro has 300 beds and the Institute Borges da Costa in Belo Horizonte has 200 beds. These along with the Aristides Maltez Institute in Bahia, and the Ofir Loiola Institute in Belem are engaged in this work. In all Brazilian states new hospitals with a total of 4,000 beds are being constructed to aid in the fight against cancer. A merger of local organizations into a single national unit will soon be accomplished. In order to carry on cancer research Brazil has already built one cyclotron, several betatrons, and several well-equipped isotope laboratories. After receiving a nuclear reactor the tempo of scientific researches in this field will be increased.

Teaching of Medicine.—The press has been instrumental in swaying public opinion in favor of the recent movement of protest of the students of the Medical University of São Paulo, supported by professors who are against the tentative increase of the number of vacancies in the university. There are 22 medical schools in Brazil, 8 of which are supported by the federal government, 7 by private endowment, 4 by the state governments, and 3 by the Catholic Church. The federal and state universities have the largest resources. The work done by these institutions is worthy of praise, thanks to the dedication and sacrifice of the professors, who maintain these organizations efficiently and honestly, in spite of serious economic problems. The medical schools run by the Church are the most recent, and their courses are well organized, although the schools are not completed yet. To maintain suitable standards the medical faculties have adopted the following principles: 1. Matriculation is limited in accordance with the size of the available teaching staff and the amount of clinical material. In January, 1955, a law of the Legislative Assembly of the State of São Paulo, corrupting this principle, was vetoed by the governor. This veto put an end to the just reaction that was provoked by the above law, in the university of São Paulo, in the congregation, in the council, and among the medical students. 2. Full-time appointments in teaching as well as in scientific research are approved. 3. The laboratories of all teaching hospitals are provided with the latest equipment. 4. A hospital internship for one year is required of graduates. 5. Postgraduate specialty training must

be regulated. There are many competent specialists in Brazil who became specialists through their own study or by taking special courses in other countries. In 1948 the Minister of Education introduced a bill for the guidance of national education. Unfortunately this bill is being blocked by the teaching commission of the chamber of deputies.

ENGLAND

Plan to Stop Air Pollution.—A national effort to free the country from air pollution in the next 10 to 15 years was urged by the Beaver Committee. It estimates that this "social and economic evil" costs the country 700 million dollars a year and wastes 10 million tons of coal. The report expresses confidence that the evil can be prevented. It must be fought with the same conviction and energy that secured clean water 100 years ago. Measures proposed are aimed at the reduction of smoke by 80% in heavily populated areas, a degree of freedom that many parts of the country have not known for over a century. This would involve cost and sacrifice. The main recommendations are: (1) a new Clean Air Act that would prohibit dark smoke from chimneys and increase penalties for smoke offenses; (2) Clean Air Council to coordinate the fight against pollution; (3) empowering local authorities to make smokeless zones in which any smoke from chimneys would be prohibited; (4) establishing larger smoke control areas in which the burning of bituminous household coal would be restricted; an exchequer grant of about 42 million dollars would have to be made for the first five years to help householders install approved appliances; (5) the requirement that all domestic heating appliances put in new homes be of approved types, and the abolition of the 50% purchase tax on gas and electric space heaters and water heaters; (6) permitting the use of no coal-fired locomotive for shunting in "black" areas after 1960 and acceleration of the program to electrify railway engines; (7) enforcement of the law against avoidable smoke from motor vehicles; (8) except in emergency, allowing no power station to operate with old and inadequate grit-arresting and dust-arresting plants or low chimneys after 1964; and (9) extension of the government's loan program for approved fuel-saving schemes to cover reduction of air pollution. This control of air pollution would cost only a fraction of the amount saved. Deaths from bronchitis are higher in Great Britain than in other European countries, and air pollution may be a factor in causing this and lung cancer. About 5,250,000 tons of sulfur dioxide, one of the most harmful pollutants, is discharged into the air each year. Research is necessary to determine the best means of preventing this, and recovering marketable sulfur now dispersed in the air.

Fewer Births and More Old Folk in Future.—A call to caterers to eliminate food poisoning was made by Sir John Charles, chief medical officer, Ministry of Health, in part 2 of his report for 1953. The cases were more numerous last year than in 1952. Unhygienic practice in the preparation and serving of food was a direct reflection on caterers. Processed, made-up, and reheated dishes were the principal causes of outbreaks.

Old people were not living much longer, but many more were now attaining the age of 65. The expectation of life at 65 in the period 1838 to 1854 was 10.8 years; in 1952 it was 12 years. The main long-term change to be expected is more old people and fewer children. We were approaching the age distribution to be expected in a stationary population with a relatively low mortality. In 1953, 22% of the population were under 15 years of age; 66% were between 15 and 64; and 11% were 65 and over. Corresponding proportions in 1901 were 32, 63, and 5%. The expected proportions in 1993 will be 20, 64, and 16%. A male infant in the period 1838 to 1854 might have been expected to live less than 40 years. By 1952 a male infant had an expectation of more than 67 years of life.

The health of the nation, as expressed in basic statistics, shows signs of becoming stabilized. It might even be that the gains likely to be yielded by the currently available means of improving health had been almost fully achieved. The present level of the birth rate is high enough for the replacement of the population. The halving since 1949 of the death rate for young women aged 15 to 19 is attributable to the great reduction in mortality from tuberculosis. The virtual disappearance of typhoid and the practical elimination of diphtheria within a decade were other noteworthy features, but the maintenance of these gains requires unremitting vigilance. On the other hand, the mysterious and inexorable march of lung cancer continued to claim an additional 1,000 victims each year. The slow improvement in the stillbirth rate suggests that a reexamination of the problems of childbirth is required. Whooping cough was more deadly to infants than any other common infectious disease. The incidence of poliomyelitis showed a shift from the younger to the later age groups.

The Medical Court of Justice.—The Disciplinary Committee of the General Medical Council has acted on accusations against several physicians. The cases include some who had been struck off the National Register, and who applied for reinstatement. Dr. Miller was restored after having been struck off in 1953 following a prison sentence for procuring an abortion. Dr. Laura W. McConnell, who was sent to prison for three years in 1936 for performing illegal operations, was restored to the register. Dr. Flanigan, who last year was found guilty of defrauding the National Health Service, was allowed to remain on the register. Applications for reinstatement were refused to S. R. Gunewardene, who was convicted in 1951 for the manslaughter of a woman; Henry C. C. Hackney, who had a number of convictions for various offenses; and Arthur J. Daly, who was struck off in 1952 following divorce proceedings in which he was concerned. Dr. Chapman appeared on charges of adultery with a married woman. The charges arose out of divorce proceedings, Chapman admitting adultery on three occasions and that she was his patient at the time. Counsel for Chapman said that steps had been taken that might enable Chapman and Mrs. Jones to marry. The disciplinary committee decided not to order his removal from the register. In the case of a physician who had supplied drugs to his wife, a drug addict, although he had twice signed an agreement not to give her drugs, and who had been fined $168 in a civil court for unlawfully possessing dangerous drugs, the committee postponed judgment for one year. A similar postponement was also made in the case of a physician who had written, signed, and issued certificates for nonpatients who desired help in obtaining houses from the Belfast Council.

Occupational Health Service.—An editorial in the *British Medical Journal* of Nov. 20, 1954, draws attention to the apparent need for an expansion of medical supervision for the worker in his place of work. The British Medical Association has recently stated its belief that the state should assume responsibility for directing the development of a national occupational health service, for exercising central supervision of such a service, preferably through the Ministry of Health, and for providing, at least in part, the necessary financial resources. The question then arises whether this service should be antonymous or be an integral part of the National Health Service. The present industrial health service, apart from factory inspections, is almost completely provided at the expense of industry, and cannot be considered independent. The tendency today is to widen the conception of occupational health. The British Medical Association believes that the time has not yet come to lay down the precise form of an occupational health service. The Minister of Labor and National Service announced in the House of Commons that after consultations with industry and with medical and other organizations he had decided to take steps to stimulate the further development of industrial health services in work places covered by the Factories Act. A standing Industrial Health Advisory Committee (on which the British Medical Association among other bodies is to be represented) will be appointed to advise the minister. Field investigations are to be carried out in order to determine the need for preventive measures or research and also to determine where the occupational health services should be extended.

Radiotherapy.—The *British Medical Journal* of Nov. 20, 1954, in an annotation describes a new linear accelerator producing 4-million-volt x-rays and a betatron producing 20-million-volt x-rays. Both machines, together with a 300 kv. deep therapy set of novel design, are housed in a special building provided by the Medical Research Council. The linear accelerator produces an x-ray beam of comparable quality with that of the gamma ray beam of a cobalt "bomb," and although the x-radiations are of a somewhat higher penetration there is not likely to be any marked difference in the results of the application of these two types of source to the treatment of cancer. The linear accelerator is capable of a much higher output than that of any cobalt source that is likely to be used, but this is of little or no practical importance, since the output of the massive cobalt units is sufficient for all practical purposes. The 4 mev. linear accelerator presents few new problems in the measurement of dosage and the planning of treatment, and it is proposed to use it immediately for the treatment of patients. The betatron, on the other hand, is the only clinical adaptation of this machine in this country, and much experimental work will have to be done before it can be applied to the treatment of patients.

A Healthy Summer.—The *British Medical Journal* of Nov. 20, 1954, comments on the summer of 1954, saying that after what has been generally condemned as one of the worst summers in living memory, it comes as something of a surprise to find that the nation has surpassed itself in breaking records for good health. If the number of patients with infectious diseases reported may be taken as a guide, they point to a population much less debilitated than usual by summer epidemics. In England and Wales diphtheria and scarlet fever both reached record low levels in the number of patients reported weekly—diphtheria with 4 cases in the 34th week and scarlet fever with 313 in the 36th. During the period April to September inclusive the total numbers of patients reported with acute pneumonia, meningococcic meningitis, typhoid, scarlet fever, and diphtheria were the lowest for the last 15 years, and only in 1944 were fewer patients with measles reported. Dysentery, on the other hand, provided a striking contrast, with the highest number of patients reported for many years.

More Low Mortality Records.—Another spotlight on mortality rates is given by the Registrar-General's Statistical Review of England and Wales for 1953 (Medical). In every age group between 5 and 55 for both sexes the death rates were the lowest recorded. There were less than 9,000 deaths from tuberculosis or about a third of the number for 1938. Mortality from most of the common infectious diseases had decreased markedly. The outstanding example was diphtheria; there were 23 deaths from this cause or less than one-hundredth of the number in 1938. Mortality from cancer generally has declined since 1938, but that from cancer of the respiratory system (over 16,000 deaths) has increased more than two and a half times in men and more than two-thirds in women.

Family Doctor Phrase Best.—Say family doctor, not general practitioner, urged Mr. Macleod, minister of health, at the annual meeting of the British Medical Students' Association in London. His young audience cheered when he said he infinitely preferred the term family doctor. It gives a much more real idea of what a physician does. "It sums up his real role of not merely skilled medical adviser but confidant and friend of the family. It is a phrase we ought to get into the habit of using."

FRANCE

Cultures of Poliomyelitis Virus.—At a meeting of the Academy of Science on Nov. 29, 1954, Prof. P. Lepine of the Pasteur Institute described a new technique for the in vitro cultures of poliomyelitis virus. In such cultures the best output is reached when all the host cells are infected. The final output depends on the number of virulent particles liberated by each infected cell. Professor Lepine uses renal cells of a simian or human origin obtained through trypsinization in suspension in a synthetic medium derived from the "635" medium enriched with animal or human serum or serum fractions, in a proportion of 0.5 to 2%. The cell cultures are placed in a flat position so as to obtain a monocellular layer, the number of which is estimated daily. After seven days of incubation the medium is changed and a suspension of the virus is introduced. The virus is fixed within an hour. In four hours cellular multiplication has practically ceased. Under optimal conditions all cells are attacked, and a few hours later the cellular destruction is complete. The virus is titrated again. This titer is divided by the number of cells in a square centimeter present at the time of inoculation. The quotient gives the number of virulent particles liberated by every infected cell. A constant average of more than 350 virulent units per cell has been observed. When the destruction of the cells is rapid and complete, this number may reach 700. Modification of the medium has no influence on the output but only on the speed with which the maximum is reached.

Eczema Cured by Hypnosis.—H. Faure and H. Berger in *Le Progrès Médical* reported the case of a 30-year-old man with an eczema of 10 years' duration. After a latent period the patient had an acute exacerbation three weeks after a severe emotional shock. He had been buried in the wreckage of a bombed building for four hours before he was rescued. The eczema reappeared with hysteriform crises, a functional paraplegia, and depression on each anniversary of the bombing. The patient was treated in a mental hospital. The electroencephalogram showed some modifications of the epileptic state. The patient was isolated and hypnotized twice with an interval of one week. The treatment was completed with a therapeutic sleep and three weeks of psychotherapy. Fifteen days after the end of the therapeutic sleep the patient was thoroughly cured of his eczema and his neurosis and the electroencephalogram had returned to normal.

New Treatment for Perlonyxis.—Side and Cohen have treated purulent perionyxis with a special preparation of hexomedin (di-isothionate of diamidino 4-4 diphenoxy-1-6 hexane, 2535 R. P.) that is not yet commercially available (*Le Concours Medical* **33**:3101, 1954). It is a mixture of an organic solvent in solution with some propyleneglycol diluted with water containing hexomedin. This solution penetrates the sebum. The authors have treated 42 such patients at the St. Louis Hospital, 25 of whom recovered in periods ranging from 15 days to six months; 12 of whom improved; and 5 of whom were not benefited. The treatment consisted of soaking the infected fingers for one to three minutes daily and in painting the other fingers with the same preparation.

New Smallpox Vaccine.—At a meeting of the Academy of Science Prof. G. Ramon and his co-workers reported that they had obtained an abundant culture of the smallpox vaccine virus in a medium made with fragments of bovine fetal skin in suspension in bovine amniotic fluid. The virus was attenuated by means of formol and heating. Injected subcutaneously this inactivated virus immunized the test animals. The authors believe this vaccine to be harmless and urge that it be used in place of the type of smallpox vaccine now in use. They believe it could be combined with poliomyelitis vaccine in immunizing young children.

MEXICO

Congress on Tuberculosis and Silicosis.—At the Sixth National Congress on Tuberculosis and Silicosis held in January in Mexico City, Dr. Alfonso Jiménez Galán reported a survey of the inhabitants of various districts of Mexico City, in which it was found that 1.4% of the persons less than 1 year old were tuberculous, as shown by radiography. In the other age groups, 1% were found to have tuberculosis. Dr. D. G. Alarcón, president of the National Committee for the Fight Against Tuberculosis, proposed that the department of health and assistance and the Mexican Institute of Social Security should work together. He recommended that the Institute of Social Security consider the problem of the tuberculous worker not only as it concerned the worker himself, but also as it concerned his close relatives until

he was completely cured. He also said that the worker is genuinely in need of help during the course of his illness because his family feels the loss of income and that each new worker applying to the Institute of Social Security for the rights of an account holder should have a roentgenogram of the chest. The worker, if found to be ill, should be sent to the National Committee for the Fight Against Tuberculosis, so that the necessary medical attention can be given him. Dr. Mauro Loyo, medical subdirector of the institute, commented that the institute was not in a position to make the 30,000 roentgenograms of the chest each month that would be needed to establish the service proposed by Dr. Alarcón. Drs. Navarro and Guerra analyzed a series of 12,127 tuberculin tests and found that 15% of the children less than 1 year old and 33% of those less than 4 years old were tuberculin positive. Radiological evidence of tuberculosis was found in 1.4% of a group of factory workers in Veracruz. Dr. Jiménez Balán reported an incidence of 1.8% among a group of field workers. Dr. Cosío Villegas stated that many patients thought to have anemia, dyspepsia, typhoid, rickets, etc., really have tuberculosis in the disseminative stage, and that no diagnosis is made, because of a lack of radiological examination or appropriate laboratory tests and, especially, because of the ignorance of many physicians of the cyclic theory of tuberculosis.

NORWAY

Homes for the Aged.—A questionnaire, sent to 547 homes for the aged by the ministry of health showed that 70% of these homes were under the administrative control of municipal authorities, but that all were under the sanitary control of the local health authorities. The inmates (about 5,000 men and 8,000 women) represented 0.4% of the total population of the country. Of these inmates, 42% needed nursing care, 12% were under the age of 65, and 6% of all the inmates (45% of those who were under the age of 65) suffered from mental debility or insanity. Prof. Axel Ström, of the Institute for Social Medicine, Oslo, finds this situation unsatisfactory, particularly with regard to the admission of so many persons with mental debility and insanity to homes primarily intended for the comfort of old folks needing the amenities of home life. The Norwegian Gerontological Society, which sponsored this survey, is conducting a campaign for improving the lot of the aged and is working on the principle that accurate information must be collected and presented to the central and local health authorities before effective pressure can be brought to bear on them for reforms. With the facts and findings presented by Professor Ström, it is now possible to reinforce the arguments for better housing accommodation for the treatment of mental disease and for answering the complaint that homes for the aged are being turned into mental hospitals to their great disadvantage.

Census of Quacks.—In the winter of 1951-1952 Dr. Henrik F. Lange had the patients admitted to the medical service of a hospital in a rural district of Norway fill out a questionnaire about their patronage of quacks after first gaining their confidence while taking down records of their present illness. They were asked to state the character of the quacks consulted as to whether they were clairvoyants, chiropractors, homeopaths, or nature doctors; the number of consultations; the time at which they were given; the reasons for seeking them; the quack's diagnosis and treatment; the results of such treatment; the opinions of the patients of it; and their reasons for preferring a quack to a physician. After discarding some as unsatisfactory, 247 questionnaires were analyzed. With 15 exceptions, the patients were adults, and among them were 75 who had sought the advice of quacks and 157 who had not done so. More than one-third of the men and less than one-third of the women patronized quacks. A tabulated list of quacks giving the number of times each was consulted was headed by a traveling homeopath with regular consultation hours. A chiropractor came next, and an "iris-diagnostician" came fourth on the list, beating by several points a clairvoyant who had had only four consultations. The ailments for which the quacks were consulted could be classified according as they were functional (pain in the back) or more tangible (polyarthritis, eczema, etc.). Among the 35 benefiting from the treatment were 28 with faith in it, and among the 32 skeptics 26 had derived no benefit from the treatment that had varied from pills and tablets to prayer and the laying on of hands. Lange, whose findings are recorded in the *Journal of the Norwegian Medical Association* for Nov. 15, 1954, found that a large percentage of the patients who had earlier sought aid in vain from a physician had apparently been helped by a quack. A survey conducted by the Norwegian Gallup Institute among 2,300 adult Norwegians showed that 25% of them believed in the gift of prophesy and that 33% had on some occasion or other consulted a clairvoyant about the future.

Slovenly Prescribing.—In the summer of 1954 the Norwegian Ministry of Health addressed a circular to physicians and pharmacists, drawing attention to the most important regulations concerned with the prescription of drugs. This action was prompted by the far too common neglect of these regulations. When they are flouted and there is trouble, it is the pharmacist who gets into trouble. Tor Njölstad, a pharmacist in charge of a medium-sized drug store in Oslo, has published in the *Journal of the Norwegian Medical Association* for Jan. 1, 1955, an account of how he obtained statistical information on this subject in September, 1954. Throughout this month he kept a record of the time spent on the telephone in checking up and correcting mistakes. Among the 2,940 prescriptions filled in this month 101 (3.4%) were faulty. In about half these cases the offending physician was not contacted on the telephone for various reasons. More than four hours were spent in telephoning to the offending physicians, who, in some cases, had to be called three or four times before contact could be made. Had all the 101 offending prescriptions prompted telephone calls, more than six hours would have been spent in this way. Prescriptions written in a slovenly manner inflict nearly an extra day's work every month on a medium-sized drug store. It might have been supposed that slovenly prescribing was the special domain of a few careless physicians, but the 101 faulty prescriptions were written by 80 physicians and the worst offender was not guilty of more than four of them. Njölstad complains that such faulty prescriptions work a hardship on the patient who has to wait while the pharmacist telephones to the physician and are a source of irritation for the physician himself who grumbles over being disturbed about what he calls trifles.

Employment of Tuberculous Persons in Industry.—Prof. Haakon Natvig of the University Institute of Hygiene in Oslo, is the industrial medical officer of an important industrial concern dealing with electrical equipment. In this capacity he is responsible for the health of the employees of this concern and among them are several tuberculous persons recommended for employment by tuberculosis specialists and other physicians holding appointments in the public health service. Professor Natvig has investigated the working capacity of these tuberculous employees who, during the eight year period beginning in 1946, numbered 119. The Norwegian Industrial Medical Officers' Council has adopted the principle that persons recovered from tuberculosis must compete on the same footing with other applicants for work. Professor Natvig found that 32 of the 119 tuberculous employees suffered from a relapse of their disease, about half of them after less than a year's employment. The tuberculous employees took much more sick leave than the nontuberculous ones. One reason for this unsatisfactory state of affairs was that far too many tuberculous persons were allowed to work before there was sufficient evidence of the arrest of their disease. On the other hand, a large number of tuberculous employees made good, and, in spite of some unhappy incidents, Professor Natvig believes that tuberculous persons can be successfully placed in industrial jobs to the advantage of all concerned. The subjects who had had operative treatment fared better than those who had been treated conservatively.

CORRESPONDENCE

AGRANULOCYTOSIS FOLLOWING USE OF CHLORPROMAZINE THERAPY

To the Editor:—I have had a patient with acute agranulocytosis with a fatal outcome that was caused, in all probability, by the use of chlorpromazine (Thorazine). The fulminating onset, typical clinical picture, and short duration of the illness were closely observed and recorded. The clinical picture was similar to agranulocytosis, sometimes observed following administration of aminopyrine. A 62-year-old woman was admitted to the hospital with a diagnosis of presenile brain disease in February, 1953. The physical examination did not reveal any abnormalities at the time of her admission. Laboratory findings were as follows: urine: no albumin, no sugar, sediment in normal ranges. Complete blood study showed 5,100,000 red blood cells per cubic millimeter, 8,400 white blood cells per cubic millimeter, and a hemoglobin level of 12 gm. per 100 cc. Kahn test was negative. Chest x-ray did not reveal any abnormalities of the heart or lungs. After admission, the patient was treated symptomatically for ankle edema, constipation, seborrhea, and disturbed behavior. She was given digitoxin, 0.1 mg. daily for two months; mercuhydrine, 1 cc. intramuscularly weekly for one month; phenobarbital, ½ grain (30 mg.) three times daily for one month; chloral hydrate, 8 cc. at bedtime, as required, for three months; and mineral oil, as required. During the treatment, repeated blood and urine studies were done. These did not reveal any abnormalities. The patient's behavior continued to be much disturbed. Therapy with chlorpromazine, 50 mg. three times daily, was instituted on Oct. 14, 1954, with the simultaneous discontinuance of all other medication.

Improvement of her mental condition was striking. She sat in a chair very quietly most of the day. She was neatly dressed and tidy. She ate well and was more cooperative. The continuous grimacing and disturbed behavior disappeared. She attended movies and watched the pictures intently and quietly. Twelve days later, on Oct. 26, 1954, chlorpromazine dosage was reduced to 50 mg. twice daily because the patient seemed to be somewhat somnolent. An allergic rash appeared on the face, neck, and upper back, and the patient was given benadryl, 50 mg. three times daily, orally, for three days, in addition to chlorpromazine. The allergic rash disappeared. The blood study done one month after chlorpromazine therapy was begun, Nov. 16, 1954, was as follows: 4,180,000 red blood cells per cubic millimeter, 8,050 white blood cells per cubic millimeter, and hemoglobin level 12.9 gm. per 100 cc. Differential Schilling blood count showed myelocytes 1, segmented 68, lymphocytes 20, and monocytes 11. Dosage of chlorpromazine was increased again to 50 mg. three times daily; therapy was continued until Dec. 5, 1954, and there were no unusual changes in her physical or mental status.

Suddenly, approximately seven weeks after treatment with chlorpromazine was begun, on Dec. 5, 1954, the patient developed a high temperature (102.2 F), great weakness, complete anorexia, and profuse perspiration. Physical examination revealed a diffuse, ulcerated tonsillitis and pharyngitis. Lung and heart were clear to percussion and auscultation. The abdomen was soft and nontender. Extremities were normal. Morphological blood study was done on Dec. 6, 1954, with the following results: 3,900,000 red blood cells per cubic millimeter, 1,500 white blood cells per cubic millimeter, and a hemoglobin level of 10 gm. per 100 cc. Schilling differential blood count showed: myelocytes 4; eosinophils 2; lymphocytes 70; monocytes 20; sedimentation rate, index 32. Urinalysis showed a specific gravity of 1.021; 3+ albumin; 1+ sugar; many granular casts in sediment. The nonprotein nitrogen level was 55.8 mg. per 100 cc. Later that day, temperature rose to 105 F. Blood pressure fell to 70/35 mm. Hg, pulse rate was 180 per minute, and breathing became rapid and superficial. The patient went into deep shock. Penicillin, 400,000 units, intramuscularly immediately; streptomycin, 1 gm. intramuscularly; 5% glucose in water given cutaneously; and oxygen given nasally were administered. Despite all of these measures, the patient died on Dec. 7, 1954, in the morning hours. Autopsy and bone marrow studies were refused by the patient's relatives.

This report describes the clinical course in a patient receiving chlorpromazine for disturbed behavior who died of agranulocytosis seven weeks after therapy with the drug was begun. Complete serial blood studies should be carried out in patients receiving this drug. Further control studies on the effects of chlorpromazine on the hematopoietic system are desirable, particularly since the drug has been felt to be relatively nontoxic to date.

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HEADACHES

To the Editor:—In the extensive literature on chlorpromazine and reserpine reports on the usefulness of these drugs in patients with headache are conspicuous by their absence. In personal communication one doctor who had reported on a series of 600 hospitalized patients stated that chlorpromazine therapy was very effective even with small doses in patients with headache. He mentioned that 0.05 gm. given intramuscularly was specific for his wife's periodic migraine attacks. A second doctor reporting on 425 patients agreed. A third doctor who had reported on reserpine in a fairly large series of cases could not answer the question. Rauwolfia has been used for headache by Indian practitioners of medicine for centuries. I prefer chlorpromazine because the former frequently causes impotence and sometimes increases the severity of depression, thus increasing the risk of suicide. I have prescribed Thorazine for nine patients presenting headache as a major complaint. I used 25 mg. three times a day in seven and 10 mg. in two cases. One of the latter, the only patient with classical migraine who experienced attacks two or three times a week, reported only one headache, which was easily relieved with Cafergot, in three weeks. The other patient reported no relief. Two of the patients receiving 25 mg. three times a day reported marked improvement, two reported moderate, one slight, and two reported no improvement in headache but less gastrointestinal reaction. On the basis of my limited experience, I believe chlorpromazine is helpful in some patients with headaches in whom the symptom was refractory to other medicaments and psychotherapy.

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SODIUM IN TAP WATER

To the Editor:—The articles by the Council on Foods and Nutrition on sodium-restricted diets in THE JOURNAL, Nov. 13, 20, 27, 1954, pages 1081, 1171, and 1252, failed to mention and stress the fact that tap water can be the source of considerable amounts of sodium in the diet. I believe this is a serious omission, inasmuch as some city tap waters have been shown to contain large amounts of sodium. Cole (*J. A. M. A.* **140**:19 [May 7] 1949) states, "The sodium content of the water must not be ignored when it is more than 10 mg. per hundred cubic centimeters, as in Aberdeen, S. D.; Biloxi, Miss.; Crandall, Galveston, and Houston, Texas; Galesburg, Ill.; Kansas City and Nevada, Mo.; Los Angeles; Marion, Ohio; Minot, N. D.; Oklahoma City; and Phoenix, Ariz." It should be noted that analysis by our laboratories of these and other city sources shows concentrations of sodium as high as 40 mg. per 100 cc. Obviously, certain tap waters can contribute large amounts of sodium to the diet and should be taken into consideration by the physician when planning a sodium-restricted diet.

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The National Research Council publication no. 325, "Sodium Restricted Diets," from which the articles appearing in THE JOURNAL *were taken, contains an extensive discussion of the*

sodium content of tap waters. This publication may be obtained from the National Research Council, 2101 Constitution Ave., N. W., Washington, D. C., for $1.00 per copy.—ED.

SUMMARIES FOR PAPERS

To the Editor:—The feature paper on page 305 of THE JOURNAL of Jan. 22, 1955, "Critical Reevaluation of Antibiotic Therapy in Surgery," illustrates a point which deserves some comment. I scanned the headings and passed up the paper, because often, I have found, a paper without a summary is one with poorly organized material. Then, after reading the editorial on page 348, I turned back and read the paper. The material is practical and well written, but a proper summary would have served me well and saved some time. My plea is that all papers in THE JOURNAL should have good summaries. This will catch more general readers and give wider spread to the subject matter, which is important with a paper like the one mentioned above.

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MAGAZINES AND BOOKS FOR ABROAD

To the Editor:—For the first time since I started to send magazines and books abroad I find myself with more material on hand than I have requests. There was some difficulty in delivery during a part of last year, and I lost some of my correspondents. I would be glad to hear from physicians abroad who are more or less isolated who do not have access to THE JOURNAL. These constitute the larger portion of the magazines saved for me to send abroad. I have no regular stock and have nothing for sale, and, as it is an unendowed and personal affair, I am somewhat limited. However, I will answer all letters sent me and particularly ask that that courtesy be returned.

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LUNG CANCER

To the Editor:—Recent articles in journals in America and England about primary lung cancer in South Africa contain two statements that to me do not seem to be in accord with facts. The first is that primary lung cancer is practically nonexistent among the South African Bantus and second that the incidence of this disease is high among uranium miners in South Africa. As radiologist to the Department of Mines and the Chamber of Mines for nearly 20 years, it has been my task to do research work on the effects of radiation on the lungs of European and non-European miners, and I think that the following extract from my M.D. thesis on "An Anthropathological Study of Primary Lung Carcinoma in Bantu Miners" will prove of interest to readers of THE JOURNAL. In the period 1916 to 1949, 11,365 pairs of lungs were examined post mortem in Bantu miners, and in 6 primary lung cancer was found. Of 8,468 cases examined post mortem in European miners, in 114 primary lung cancer was found. The reasons given for this variation in incidence are: 1. Bantus are "minimal smokers" of cigarettes. 2. They die at an earlier age. 3. With the exception of the liver and a few other sites, carcinoma occurs less commonly in the non-European. It is of interest to note that: 1. In recent years there has been an increase in the number of cases of this disease found in non-European miners. 2. In a big city like Johannesburg the incidence in the Bantu population was much higher, and in 1950 there were eight deaths from primary lung cancer. Some research workers believe that there may be "mutual antagonism" between the occurrence of tuberculosis and cancer in the lung, and I can quote the following statistics. "During the period 1916 to 1948 there occurred 32,269 cases of Tuberculosis with a prevalence rate of approximately 4 per 1,000 of all Bantu miners whilst there were 1,268 cases of Tuberculosis in European miners and here the prevalence rate was .78 per 1,000."

In the case of Europeans who have worked on gold and uranium mines the figures already quoted show that of all post mortems performed, in approximately 1.35% primary lung cancer was found. Among the European males over the age of 20 who have died at the Johannesburg General Hospital, over 3% of the total autopsies performed showed evidence of this disease. In addition statistics kept over a number of years at the Silicosis Medical Bureau show that the development of a definite condition of silicosis does not appear to aggravate the risk of occurrence of lung cancer. While carcinoma of the lung is comparatively rare in the Bantu, radiologists in South Africa now find that in the Bantu there is a high incidence of cancer of the maxillary antrum. As most of the Bantu smoke very little and as most of the patients with antral carcinoma have inhaled snuff in fairly large quantities and over a prolonged period of time, it has suggested that snuff taking may be a predisposing factor.

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MODERN GRANDMA

To the Editor:—After reading the poem at the end of the article, "Our Common Aims," by James Musatti in THE JOURNAL, Feb. 12, 1955, page 588, the following poem seems appropriate:

Grandma didn't have a telephone
And didn't have the urge to roam
She never saw a motor car
Nor played the golf course under par.

Her dresses were few, and each for a reason,
She didn't have a wardrobe for each season.
The only salesmen she ever met
Was the one who sold the wedding set.

Coffee she served once a day, seldom more,
Instead of at 10 and 2 and 4.
She did not paint her face or style her hair
She took time to keep the kids fair and square.

There were no clubs or parties to plague her
She looked to Sunday church, her husband to take her
And to the big chicken dinner that afternoon.
At night she was contented to watch the moon.

But modern grandma likes to smoke
And thinks homebodies are a joke,
She thinks her daughter's kids are swell
But baby sitting for them is just plain hell;

She would rather visit and go away
Tell the story of another day
When "grandmother on a winter's day
Milked the cows and fed them hay."

What grandma does she tell about?
Perhaps she thinks 'tis she, no doubt
I'll wager that it's just a dream
For grandma today has always had a washing machine.

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TOBACCO AND CANCER

To the Editor:—In a letter that appeared in THE JOURNAL, Jan. 15, 1955, page 268, Dr. L. H. Garland attempts to defend the tobacco habit by misinterpreting the statistics compiled by Drs. Hammond and Horn. In all fairness, Dr. Garland's statement that "99,761 out of every 100,000 heavy smokers aged 50 to 69 are unlikely to die of lung cancer" should have the added limitation "within a 20-month period," as this was the approximate period of observation in the study referred to. If one assumes that the death rate due to lung cancer observed in the 20-month period continued throughout a 20-year period between the ages of 50 and 69, there would be a total of 2,868 deaths per 100,000, or 1 in every 34 males. Obviously these figures offer little consolation to the heavy smoker.

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GOVERNMENT SERVICES

ARMY

Promotions in Army Medical Corps Reserve.—In a ceremony in the Surgeon General's office in Washington, Feb. 15, Brig. Gen. Isidor S. Ravdin, professor of surgery at the University of Pennsylvania, received the two stars of a major general in the Army Medical Corps Reserve, his promotion to that rank being the first achieved by a Medical Corps officer on inactive duty. General Ravdin was commissioned a lieutenant colonel on Oct. 28, 1940. From May, 1942, to April, 1945, he served as chief of the surgical service and as commanding officer of the 20th General Hospital in the China-India-Burma Theater, for which service he was awarded the Bronze Star, the Legion of Merit with Oak Leaf Cluster, and China's Order of Cloud and Banner, First Degree. When relieved from active duty on Dec. 29, 1945, he returned to the University of Pennsylvania but continued serving as a member of the Armed Forces Medical Policy Council, as a consultant to the Army Surgeon General, and as a member of many advisory committees. General Ravdin was born in 1894 in Evansville, Ind. He served his internship at the University of Pennsylvania and remained to teach, progressing from an instructor in 1920 to Harrison Professor of Surgery in 1935, John Rhea Barton Professor of Surgery in 1945, professor of surgery at the Graduate School of Medicine, director of the Harrison Department of Surgical Research, and surgeon-in-chief of the hospital of the university.

Dr. James B. Mason is a new brigadier general in the Army Medical Corps Reserve. In 1940 he was called to active duty as unit instructor to the 304th Medical Regiment, 79th Division, and to the medical reservists in Philadelphia. In 1942 he became chief of the Operations Division in the Office of the Chief Surgeon in the European Theater. In 1944 he was appointed Deputy Surgeon and later Inspector General of that theater. His last active duty tour, four years as Special Assistant to the Army Surgeon General, terminated Nov. 1, 1954. He is now the Director of Professional Education and Accreditation of the American College of Surgeons, Chicago.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Advisory Committee to Social Security Administration.—A medical advisory committee, set up to advise the Social Security Administration on medical aspects of administering the new "disability freeze" provision in the social security law, was announced Feb. 8 by Charles I. Schottland, Commissioner of Social Security. Dr. J. Duffy Hancock, professor of clinical surgery, University of Louisville School of Medicine, has accepted the chairmanship of the committee. Dr. Hancock is president of the Southeastern Surgical Congress. He has received a number of medical awards, including the Woodstock medal, presented by the University of Louisville; the E. M. Howard medal, presented by the Kentucky State Medical Association; and the American Cancer Society award for distinction in service. He holds the Bronze Star, the French *Croix de guerre*, and other decorations for his service in Europe during World War II.

The "disability freeze" provision is similar to the waiver of premium in commercial life insurance and permits a worker to keep his Old-Age and Survivors Insurance rights intact when he is totally disabled for work for an extended period. The medical advisory committee will help the Bureau of Old-Age and Survivors Insurance to set up guides and procedures for obtaining and interpreting medical evidence as to existence and extent of disability, Mr. Schottland said. These guides and procedures will be followed by the agencies in all states that have entered into the agreements to insure disabled workers all over the nation equal treatment under the law.

The committee, which held its first meeting in Washington, Feb. 9-10, includes, in addition to Dr. Hancock: Dr. Alexander P. Aitken, clinical professor of orthopedic surgery, Tufts Medical College, and director, Liberty Mutual Rehabilitation Center, Boston, Mass.; Miss Pearl Bierman, consultant in medical social work with the American Public Welfare Association, Chicago; Dr. Donald Covalt, associate professor, department of physical medicine and rehabilitation, New York University College of Medicine; Dr. Charles L. Farrell, Pawtucket, R. I., president-elect of the Conference of Presidents and Other Officers of State Medical Associations; Dr. J. S. Felton, associate professor, department of medicine and department of preventive medicine, University of Oklahoma; Dr. Herman E. Hilleboe, Commissioner, New York State Department of Health; Dr. Lemuel C. McGee, medical director, Hercules Power Company, Wilmington, Del.; Dr. Kenneth E. McIntyre, director, United Automobile Workers, CIO Health Institute, Detroit; Dr. William A. Pettit, state supervising ophthalmologist, California Department of Public Welfare at Los Angeles; Dr. Leo Price, director, Union Health Center, International Ladies Garment Workers Union, New York; Dr. W. H. Scoins, chief medical director, Lincoln National Life Insurance Company; Carroll Shartle, Ph.D., professor of psychology, Ohio State University; Mr. Byron Smith, member, board of trustees, American Foundation for the Blind, and executive secretary of the Minneapolis Society for the Blind; and Dr. David Wade, medical consultant, Texas Division of Vocational Rehabilitation, Austin, Texas.

DEPARTMENT OF DEFENSE

Credit for Attending Aero Medical Association Meeting.—Reserve credit points may be earned by reserve officers of the military medical services for attending the daily scientific sessions of the annual meeting of the Aero Medical Association at the Statler Hotel, Washington, D. C., March 21-23. More than half of the meeting's 40 scientific presentations will be devoted to military aspects of aviation medicine and flying safety, according to Brig. Gen. Otis O. Benson Jr., U. S. A. F., president of the association. A symposium on the newest developments in space medicine and a round-table discussion of the aeromedical aspects of flight at extreme speed and altitude will be presented by a group of outstanding test pilots. The first Louis H. Bauer Lecture, established in honor of the association's founder and first commandant of the U. S. Air Service School of Aviation Medicine, will be presented March 21 by John F. Fulton, M.D., Yale University physiologist. Sen. Stuart Symington, Missouri, who served as first Secretary of the Air Force, will be principal speaker at the annual dinner, March 23.

PUBLIC HEALTH SERVICE

Regular Corps Examinations for Medical Officers.—A competitive examination for appointment of medical officers to the regular corps of the United States Public Health Service will be held in various places throughout the country June 7-9. Appointments provide opportunities for career service in clinical medicine, research, and public health. They will be made in the ranks of assistant and senior assistant, equivalent to Navy ranks of lieutenant (j. g.) and lieutenant respectively. Entrance pay for an assistant surgeon with dependents is $6,017 per annum and for senior assistant surgeon with dependents, $6,918. Provisions are made for promotions at regular intervals. Active duty as a Public Health Service officer fuifills the obligation of Selective Service.

Requirements for both ranks are U. S. citizenship, age of at least 21 years, and graduation from a recognized school of medicine. For the rank of assistant surgeon, at least seven years of collegiate and professional training and appropriate experience are needed, and, for senior assistant surgeon, at least 10 years of collegiate and professional training and appropriate experience are needed. Entrance examinations will include an oral interview, physical examination, and comprehensive objective examinations in the professional field. Application forms may be obtained by writing to the Chief, Division of Personnel, Public Health Service, Washington 25, D. C. Completed application forms must be received in the Division of Personnel no later than May 6, 1955.

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

ANNUAL LIST OF POSTGRADUATE COURSES

The Council on Medical Education and Hospitals desires to announce that hereafter a single annual listing of postgraduate courses for practicing physicians will be published in THE JOURNAL rather than the semiannual listing that has been utilized in the past. The first annual listing will appear in the July 23, 1955, issue of THE JOURNAL and will cover the period from Sept. 1, 1955, to Aug. 31, 1956. It is suggested, therefore, that any institutions or organizations planning to conduct postgraduate courses for practicing physicians during this period, and who have not had their courses listed in THE JOURNAL previously, communicate with the Council for the necessary information forms on which data are to be submitted for listing. These forms are now available. It is requested that data be submitted prior to May 1, 1955, and at an earlier date if available.

LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Malpractice: Statute of Limitations—Fraudulent Concealment of Cause of Action.—The plaintiff sued the Crossett Health Center for damages for injuries allegedly caused by the negligence of its employees. Judgment was entered for the plaintiff, and the defendant appealed to the Supreme Court of Arkansas.

The Crossett Health Center was a not-for-profit corporation, which was organized primarily by the owners of a large lumber business. In July of 1948, the plaintiff was operated on at the center for intestinal adhesions and other ailments. Steel wire was used in closing the operational wound in the abdomen. After the operation the plaintiff continued to have so much pain that an attempt was made to remove the suture wire. This did not bring relief, however, and subsequently the plaintiff went to a surgeon in Louisiana, who located and removed a small piece of the suture wire from plaintiff's intestine.

On appeal the Supreme Court considered two distinct defenses, each of which the defendant claimed was a complete bar to the plaintiff's suit. The first one was that the suit was commenced well over two years after the cause of action arose, whereas an Arkansas statute provided that such an action must be brought within two years after its accrual. The court admitted that the action had arisen more than two years before but stated that under the decisions of previous cases the statute would not run if the cause of action had been fraudulently concealed by the defendant. The Supreme Court held that, if the employees of the center had not used reasonable diligence in determining the cause of the plaintiff's postoperative pains and had thereby failed to inform her of the facts on which she subsequently based her suit, the jury would have been entitled to find that the defendant had fraudulently concealed from the plaintiff her cause of action. The court concluded that the jury had been properly instructed on this point and that the evidence substantiated its finding in favor of the plaintiff.

The second defense was that the defendant was a not-for-profit corporation dispensing charitable services to various members of the community and was therefore immune from suit as a charitable institution. The Supreme Court said that in Arkansas the rule had been established that the property of a charitable organization is not subject to execution (i. e., a forced legal sale) in satisfaction of money judgments against it. The court held, however, that the center could not be treated as a charitable organization since (1) the plaintiff had been a paying patient, (2) the founders of the corporation received an indirect benefit from its existence because it was organized primarily to afford services to the employees of businesses owned by the founders, and (3) under its charter the assets of the center were not absolutely dedicated to public use.

Accordingly, the Supreme Court affirmed the judgment for the plaintiff against the center. *Crossett Health Center v. Croswell, 256 S. W. (2d) 548 (Ark., 1953).*

Malpractice: Applicability of Res Ipsa Loquitur to Physicians.—The plaintiff sued for damages for injuries caused by the alleged malpractice of the defendant surgeon. From a directed verdict in favor of the defendant, the plaintiff appealed to the Supreme Court of Indiana.

The defendant operated on the plaintiff to remove stones from the common bile duct and gallbladder. A few months later a corrective operation was necessary because a hernia had developed in the operative wound. During this operation it was discovered that the intestine was out of position and involved in a fibrous mass of skin, fascia, and peritoneum. While dissecting through this mass, the defendant accidentally perforated the plaintiff's intestine. Although this perforation was immediately sewed up and the operation completed, a fecal fistula subsequently developed. The plaintiff contended that the defendant was negligent and that the doctrine of res ipsa loquitur applied to this case.

In the absence of a special contract, said the Supreme Court, a surgeon is not an insurer and does not bind himself to make a correct diagnosis or effect a cure. An injured patient may recover damages only if he can establish that the surgeon either did not have the reasonable or ordinary qualifications of his profession or, being a specialist, did not exercise the degree of skill and knowledge possessed by surgeons who devote special attention to such ailments and treatments in light of the scientific knowledge in similar localities generally. Proof of these factors must come from accredited physicians and surgeons. The plaintiff's evidence did not establish such negligence.

The Supreme Court also considered whether or not the plaintiff could rely on the doctrine of res ipsa loquitur to establish a prima facie case of negligence on the part of the defendant. The court held that res ipsa loquitur could not be applied in this case because the surgeon was not an insurer and that the plaintiff, therefore, had the burden of clearly proving the defendant's negligence.

Accordingly, the judgment in favor of the defendant surgeon was affirmed. *Worster v. Caylor, 110 N. E. (2d) 337 (Ind., 1953).*

Nurses: As Agent of Hospital or Surgeon During Operation.—The plaintiff sued the defendant religious corporation for injuries sustained from the negligence of a nurse employed in the Stillwater Municipal Hospital, which it leased and operated. Judgment was entered for the defendant, and the plaintiff appealed to the Supreme Court of Oklahoma.

The plaintiff entered the Stillwater Municipal Hospital as a patient of her personal physician for the purpose of undergoing an operation. She was taken to the operating room, where the surgeon administered a "spinal block" anesthetic. The surgeon then left the room to scrub up. While he was out of the room a nurse in the general employ of the defendant placed the plaintiff's legs in stirrups and lowered the drop-leaf half of the operating table, leaving the lower half of the plaintiff's body supported entirely by the stirrups. She then discovered that the stirrup straps were reversed, and in attempting to correct that situation without raising the drop-leaf section of the table she let the plaintiff slide off the table onto the floor, thus causing the injuries complained of. The trial court directed a verdict for the defendant on the theory that the evidence showed that at the time of the accident the nurse was acting as the servant of the surgeon rather than as servant of the hospital.

The Supreme Court said that the question of whose servant the nurse was when she performed the negligent act was an issue of fact, which should have been decided by the jury rather than by the trial court. Generally, the court pointed out, a nurse performs her functions as a servant of the hospital. This general principle would not prevail, however, where it is shown that, as to particular acts, the nurse acted in response to directions, or under the supervision, of the operating surgeon, but the Supreme Court refused to hold, as a matter of law, that the surgeon is in control of and supervises all a nurse does in the operating room. The facts of each individual case must be left up to the jury.

The court therefore reversed the judgment in favor of the hospital and remanded the case for a new trial. *McCowen v. Sisters of Precious Blood of Enid, 253 P. (2d) 830 (Okla., 1953).*

Narcotics: Possession of Hypodermic Syringe; Unlawful Search and Seizures.—The defendant was convicted of possessing a hypodermic syringe and a rubber hose used in administering habit-forming drugs; mere possession of both items was prohibited by the Maryland narcotics laws. From such conviction he appealed to the court of appeals of Maryland.

The defendant was stopped in the evening by a police officer on the public streets in Baltimore. The officer searched him and found a doctor's prescription for 35 morphine tablets, ¼ grain each, which was made out for another person. After arresting him officers went to his apartment, where they found a rubber hose, a needle holder, a hypodermic syringe containing traces of derivatives of opium, and two empty vials. At the trial all of these items (including the prescription) were put into evidence, even though they had been obtained by state officials without a search warrant. The defendant contended this was in violation of his constitutional guarantees against unlawful searches and seizures.

The court of appeals noted that, while one Maryland statute generally prohibits the use of illegally seized evidence in criminal prosecutions, another statute expressly makes an exception to the general rule in prosecutions of violations of the narcotics laws. Thus the evidence was admissible unless its admission violated some constitutional right of the defendant. The court pointed out that it had already been decided by Maryland courts, and by the United States Supreme Court, that evidence may be used in state criminal prosecutions even though such evidence was seized in violation of constitutional guarantees. The court acknowledged that there is an exception to this rule based on facts that show that a seizure was made in a brutal or unconscionable manner so as to make the use of the evidence a violation of due process of law. But, the court held that such facts were not present in the instant case.

Accordingly, the defendant's conviction was affirmed. *Stevens v. State, 95 A. (2d) 877 (Md., 1953).*

MISCELLANY

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THE "UTOPIA" OF SOCIALIZED MEDICINE

There is no question but that living under socialized medicine is a "great" experience, if you confine the connotations of the term to vast, massive or overwhelming. Socialized medicine is all of that on many counts, particularly overwhelming.

First in magnitude, of course, is that it gives the people all kinds of health and medical service "for nothing," after first, however, taking away from the people at large in taxes, three times what this service would cost when supplied by private doctors, even though performed by them in an efficient and impartial manner, which it woefully is not, under socialized medicine.

Like everything else that the government gives to anybody, it never gives you anything for "nothing" unless it also gives you along with it a "great" deal of government control and domination. It also, happily from the standpoint of a power aspiring governmental regime, gradually, but effectively conditions you for full scale governmental dictation in all other respects.

Until you get used to it however—get used to waiting for days for the doctor to come—you don't find the "service" too satisfactory. Particularly when the harried and greatly overworked government doctor does finally get there, and is in no mood or physical or mental condition to provide you with very much of a diagnosis, prognosis or anything else.

Of course, under socialized medicine, the government "cures" everything for you from corns to dandruff, and gives you "for free," everything from hand lotion to hair dye—that is under certain conditions, and therein lies the "rub," whether it be liniment, ill-fitting free false choppers or abrading shoulder braces.

Even after you get the free splints, crutches or knee-pads you are not through with strict governmental control—that is if you hope ever to get any free medical attention again.

For instance, the *Wall Street Journal* cites the case of a young man in Leicester, England, who went in swimming and lost a set of false teeth, which he got "for free" under Britain's National Socialized Health Program. His application for a second set (he had had the first for three years and they were pretty well worn in spots), was turned down on the ludicrous ground that he had "exercised lack of care and good judgment in swimming in a rough sea."

The socialized health council had not elicited anything but this very perfunctory information and wholly ignored the possibility that there might have been extenuating circumstances.

As the *Wall Street Journal* logically enough contemplates, "this ruling raises some interesting questions. Was the sea rough when the man first went in or did it become rough later? Is that particular stretch of beach always rough, and are the nearby beaches to be denied all wearers of government teeth? Is it careless or not to proceed about London's streets during one of that city's many mists? It seems to us that to rule that a man may be denied another toupee because he lost the first the government gave him in a high wind, is to say that government responsibility in the matter of toupees and teeth should go so far and no farther. But to say that is to question the whole scheme of socialized medicine. For someone is bound to ask, as in the case of the young man from Leicester, how in the world did he lose his own teeth in the first place?"

We would add that we believe that this inflexibly enforced perpetual responsibility for the perpetuity of government incisormolars and synthetic hirsute adornment is particularly unjust in such cases as that of the young man from Leicester whose bureaucratic masticators were virtually worn out, or in the case of a man who gets caught in a sudden summer squall and loses a toupee that is very ratty and badly frayed and in fact is well over-due for a replacement.

We would respectfully add a case recently reported where an Englishman got some free medicine for a bad cold and when he came back a couple of weeks later with a recurrence of "aggravated coryza," he was refused any more medicine because he used poor judgment in getting out in inclement weather and getting his feet wet. It was not until a neighbor reported that he had pneumonia that the health bureau decided to cut the bureaucratic red tape. The belated medicine didn't do much good then however, because the next day the man was dead.

We can see where a system where you can get "for free" everything from shoulder braces to delousing lotion would be pretty tempting. However, for our part, we believe that we would still rather continue to pay our own medical expenses (even though admittedly they come high), and have something to say about whether we are going to go tooth-less, toupee-less or life-less. After all, in the latter eventuality, we somehow cannot get much consolation, even though everything therein costs you "nothing" —including the funeral expenses.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

ACTH and Cortisone in the Treatment of Asthma. H. S. Baldwin, P. F. deGara, A. D. Spielman and M. Dworetzky. J. Allergy **26**:44-53 (Jan.) 1955 [St. Louis].

Corticotropin or cortisone was given to 25 male and 35 female patients between the ages of 6 and 70 years with severe status asthmaticus who had failed to respond to the usual management. The initial dosage of corticotropin in the form of HP Acthar gel was 40 units every 4 hours for the first 24 hours. As improvement appeared, the interval was increased to six hours. Usually within a week the patients were doing well on 40 units every 12 hours. From then on, depending on the progress of the patient, the dose was lowered to 40 units daily for several days, then 40 units every other day; and gradually the point of minimum maintenance dose was reached or administration of the hormone discontinued completely. With cortisone, the dose usually effective was 100 mg. every 4 hours for the first 24 hours and every 6 hours the second 24 hours. Then 100 mg. was given every eight hours, and within a week the patient was usually doing well with 25 mg. three to four times a day. From then on, depending on the progress of the patient, the dosage was gradually cut to the amount necessary to keep the patient comfortable or the hormone was discontinued completely. Thirty of the 60 patients continued to require some maintenance with one or the other of the hormones, following the institution of this form of treatment. The remaining 30 patients required hormone therapy only for intermittent relapse. The largest amounts of the hormones administered to individual patients were 62 gm. of cortisone and 7,780 units of HP Acthar gel respectively. The longest continuous treatment given to any single patient extended over 39 months. Combined or alternating treatment with the two hormones was used successfully in 24 patients. Satisfactory results were obtained in 52 patients (87%). Only eight patients (13%) failed to respond clinically or were unable to take the hormones because of complications, such as increase of edema in advanced cardiac pulmonary disease, depression, and development of peripheral vascular thrombi in Raynaud's syndrome. Seven of the 60 patients died, but only 2 of them were receiving hormones, and those in small doses, at the time of death. Caution must be exercised in attributing too much importance to the Thorne test as a sole criterion of adrenal function or as a criterion of clinical response to either of the hormones in the management of asthma. Respiratory function tests are a useful guide to hormone therapy, but clinical improvement is more significant. In several patients, judging from the results of respiratory function tests, the progress of cardiac-pulmonary disease was apparently delayed through the use of HP Acthar gel or cortisone. During the use of the hormones, awareness of the occurrence of intercurrent infection is most important, and the use of antibiotics in this connection, together with the hormones, may be a lifesaving measure. Need of over-all management of patients with asthma is emphasized. With proper precautions, corticotropin and cortisone may be used to relieve acute attacks and also may be employed over prolonged periods with resulting pronounced clinical relief to the asthmatic state.

The place of publication of the periodicals appears in brackets preceding each abstract.

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Pneumococcal Pneumonia Treated with Antibiotics: The Prognostic Significance of Certain Clinical Findings. T. E. Van Metre Jr. New England J. Med. **251**:1048-1052 (Dec. 23) 1954 [Boston].

Data collected from large series of nonspecifically treated cases of pneumococcic pneumonia showed that an increased mortality is associated with increasing age, chronic alcoholism, the presence of concomitant disease, certain types of pneumococci, bacteremia, multilobar involvement, and a low white cell count. There is evidence that some of these clinical findings have an effect on mortality in antibiotic-treated lobar pneumonia. The study reported here was begun to obtain more information on the effect of these clinical findings on both mortality and slow recovery in antibiotic-treated pneumococcic pneumonia. The material consists of 358 cases of pneumococcic pneumonia observed at the Johns Hopkins Hospital between July, 1946, and June, 1952. The evidence presented indicates clearly that, in antibiotic-treated pneumococcic pneumonia, increasing age, concomitant disease, multilobar involvement, pneumococcic bacteremia, leukopenia, and infections due to type 1 and 3 pneumococcus are associated with increased mortality. In nonfatal cases with increasing age, chronic alcoholism, multilobar involvement, pneumococcic bacteremia, leukopenia, or infections due to types 2 and 3 pneumococcus, recovery is slower and suppurative complications more frequent. Individual analysis of the fatal cases of antibiotic-treated pneumococcic pneumonia reveals that more than one of these unfavorable prognostic signs existed in most of the patients who died.

Incidence, Characteristics, and Treatment of Child and Adult Tuberculous Meningitis Caused by Tubercle Bacilli Initially Resistant in Varying Degrees to Streptomycin. A. Degli Esposti. Clin. pediat. **36**:677-694 (Sept.) 1954 (In Italian) [Bologna, Italy].

From February, 1947, to October, 1952, a total of 287 patients with tuberculous meningitis was admitted to the Pediatric Clinic of the University of Bologna. In only 0.69% of these was the disease caused by tubercle bacilli that were initially more or less resistant to streptomycin. From October, 1952, to October, 1953, there were 48 such admissions, and the disease was caused by streptomycin-resistant bacilli in 37.5% of these. Strains that were not inhibited by at least 10 gamma of the antibiotic per 1 cc. of culture were considered resistant. Tuberculous meningitis caused by streptomycin-resistant bacilli was less common in adults than in children (29.3% as against 59%), and in these it was commoner among the younger ones in whom the contact was assumed to have occurred more recently with respect to the time of admission. Some of the patients had received the antibiotic previously, but, because it was given only for a few days before their hospitalization, it is doubtful that the short treatment could have had by itself any influence on the degree of resistance of the bacilli. Degli Esposti deduced that most of the patients in this group had become infected with strains of bacilli that had already developed resistance to the antibiotic. He ascribes the increase of the last years in the cases of tuberculous meningitis caused by such bacilli to unnecessary, indiscriminate, and sometimes inadequate use of antibiotics. He feels that today more than ever preventive antituberculous vaccination of the newborn infant should be used. This view seems to be supported by the fact that not one case of tuberculous meningitis was observed among 12,000 children who had been vaccinated at the Vaccine Prophylactic Center of the University of Bologna. The course of the disease was particularly grave in the children. In these the meningitis was at first localized and asymptomatic and without signs of tuberculous toxemia, but the latent lesions progressed to reach proportions that caused the violent course of the disease. In all

the children, even in the nurslings, the lesions of the tracheobronchial lymph nodes were mainly of the productive type and with little caseation, much unlike those that are generally found in nurslings with this disease. Prognosis for these children is unfavorable. All those in the first five years of life died despite the early use of isoniazid. In adults the infection was localized in the choroid plexuses of the lateral ventricles and as such it did not cause sudden alterations in the circulation of the spinal fluid, and the course was less grave. Tuberculous meningitis caused by strains of bacilli that are more or less resistant to streptomycin should be treated by isoniazid given parenterally or intrathecally. The treatment should always be individualized.

Clinical Course and Treatment of Tuberculous Meningitis in Childhood: Report on Experiences Between 1948 and 1954 of the Pediatric Clinic in Freiburg. F. E. Struwe and O. Vollmer. Beitr. Klin. Tuberk. **112:**363-377 (No. 5) 1954 (In German) [Berlin, Germany].

Of 78 children with tuberculous meningitis who were treated at the pediatric clinic of the University of Freiburg, Germany, between 1948 and 1954, 34 were boys and 44 girls. Up to June, 1949, treatment consisted of intramuscular administration of 0.04 gm. of streptomycin per kilogram of body weight daily and of intrathecal administration of 0.05 gm. of streptomycin daily. Since July, 1949, oral administration of 0.3 gm. of *p*-aminosalicylic acid per kilogram of body weight was added. Since July, 1950, newly admitted children were given "prolonged" treatment by intramuscular administration of 0.02 to 0.03 gm. of streptomycin per kilogram of body weight daily and 0.02 to 0.03 gm. of streptomycin intrathecally daily. From July, 1952, to March, 1954, treatment consisted of intramuscular administration of 0.04 to 0.05 gm. of streptomycin per kilogram of body weight daily in two divided doses, 2 to 3 mg. of streptomycin per kilogram of body weight intrathecally daily, oral administration of 0.3 gm. of *p*-aminosalicylic acid per kilogram of body weight daily, and one-hundredth of this dose (maximum 0.06 gm. per day) intrathecally; to insure therapeutic success, this was followed by oral administration of 0.01 gm. of isoniazid per kilogram of body weight. Vitamin C and vitamin B complex, as well as standardized cod liver oil, were used as adjuncts to chemotherapy. The duration of the treatment depended on objective findings. Lowering of cell numbers, reduction of increased proteins, and normalization of colloid curves were considered as criteria of therapeutic success. After discontinuation of the intrathecal administration, treatment was continued for three to four months with a tuberculostatic agent that had not yet been used or only little and was followed up by current examinations of the cerebrospinal fluid; those patients in whom therapeutic success was maintained were then moved to a children's sanatorium in the Black Forest for a three months' rest in fresh air followed by control examinations at intervals of three months. The patients were subdivided in five groups. Group 1 consisted of nine children who died within the first 10 days after admission. The second group comprised eight children who died within the first six weeks after admission, and in none of them was a definite therapeutic success observed; only three showed temporary improvement. All eight patients had characteristic cerebrospinal fluid findings, with predominantly lymphocytic pleocytosis of 93 to 736 cells, low sugar levels of 15 mg. per 100 cc. of cerebrospinal fluid, and abnormal colloid curves. The third group consisted of 17 children who died later than six weeks after admission while under treatment or shortly after treatment was terminated. Nine of these 17 patients had pareses or hemipareses of extremities, rigor, extensor spasms, tremor, athetosic movements, nystagmus, loss of papillary reflexes, or rolling disease caused by vascularly conditioned foci of softening in the area of the basal ganglions and the internal capsule. Cerebral pressure symptoms became predominant, and general deterioration resulted in cachexia and regulatory failure associated with bronchopneumonia. The fourth group consisted of 38 children who recovered; 22 of the 38 did not have any significant defects, 11 had defects of moderate degree that appeared to be compensatable to a large degree, and 5 had severe defects resulting from encephalopathic involvement: they had serious mental disorders and massive neurological findings. The fifth group consisted of six children; one, a 13-year-old boy, died suddenly, probably from cerebral hemorrhage, 21 months after his discharge. The remaining five are still under treatment. Prognosis of tuberculous meningitis in childhood becomes more favorable in older children and more unfavorable with prolonged duration of symptoms before the institution of treatment. Survival and restoration to normal depends to a large extent on the presence, new occurrence, and extent of foci of softening in the area of the basal ganglions. The recovery rate was considerably improved by the combined intrathecal administration of streptomycin and *p*-aminosalicylic acid, and that as a result of the reduced number of late fatalaties. The duration of the intrathecal treatment, however, could not be shortened by the improved technique but on the contrary had to be prolonged as compared to 1948-1949; 160 to 360 days of the combined intrathecal treatment were required for recovery as compared to 90 to 120 days with the earlier technique. Thus more time and a larger amount of drugs are necessary to guarantee therapeutic success.

Experiences in the Management of Long-Standing Chronic Cases of Pulmonary Tuberculosis Treated with Isoniazid for One Year. H. T. Overby and R. W. Woliung. Dis. Chest **29:** 51-58 (Jan.) 1955 [Chicago].

The effect of isoniazid on tuberculous patients in the "maximum benefit" or "good chronic" category, i. e., those with extensive pulmonary tuberculosis of many years' duration who have apparently received the maximum benefit from hospitalization but whose discharge cannot be considered in keeping with public health policies, was studied in an investigation conducted at the Dunham Hospital, Cincinnati. Most of the 38 patients in the study group had histories of long hospitalization prior to the commencement of the study (average length of previous hospitalization, 37 months), and 21 had had more than one previous admission to this hospital (patients in this category often leave the hospital against medical advice because they feel hopeless and neglected). Streptomycin in combination with *p*-aminosalicylic acid had previously been given to 24 of the patients and in some cases the courses had been quite intensive and prolonged, 2 patients having received 323 and 241 gm. of streptomycin with *p*-aminosalicylic acid respectively. Isoniazid dosage at first consisted of 250 mg. daily given orally in two doses; later, this was changed to 300 mg. daily, given in three doses, merely as a matter of convenience because the medication, originally supplied in 50 mg. tablets, was then being supplied in tablets of 100 mg. each. The patients' subjective symptoms were evaluated once each month and their weight was recorded weekly. Sputum studies were made each month and roentgenologic comparisons every three months. Marked improvement in subjective symptoms, such as morale and sense of well-being, was noted from the beginning. Increase in appetite and weight gain were pronounced, and there was a decided reduction in cough and volume of sputum, paralleled by a sharp reduction in the consumption of cough medicine. Chest roentgenogram shadow improvement, though definite, lagged behind clinical improvement for the most part; by the end of a year, however, six patients whose prognosis for cure had been considered poor were discharged from the hospital with their disease arrested and with negative sputum. A marked decrease in the incidence of positive sputums, which fell from 94% before therapy to less than 50% during any subsequent month, was observed soon after the treatment was started, and this decrease, which is important from the standpoint of public health because it makes those patients who leave the hospital against advice potentially less dangerous as a source of infection, was maintained throughout the year, although in some cases sputums that had become negative became positive again. The clinical improvement reflected in these findings shows that isoniazid alone may prove therapeutically effective in the institutional management of "good chronic" cases of pulmonary tuberculosis in which other forms of therapy have failed.

Observation on BCG Vaccination of Nurses. P. D. Kannivelu. Indian M. Gaz. **89**:275-282 (May) 1954 [Calcutta, India].

A report was made on the results of tuberculin tests (Mantoux) and BCG vaccination in 743 student nurses, 594 female and 149 male, from the state of Madras, India. They ranged in age from 17 to 25 years for the most part, and came from both urban and rural areas. No conclusions were drawn concerning the morbidity and mortality attendant to BCG. The following statements were made, however. Tuberculin sensitivity varies directly with increasing age. It also increases with years of training of these nurses. There is virtually no difference in the percentage of reactors among the sexes. The severity of tuberculin reactions in the natural reactors does not seem to signify anything in particular. Complications of BCG vaccination are almost negligible. The allergy after vaccination was normally comparatively weaker, with declining intensity from year to year unless there was a superinfection. The allergy after vaccination was maintained in the majority of the nurses for a long period (90% of them retained allergy for at least three years). Violent reactions to retests are rarely seen after BCG vaccination, unlike those in the case of natural reactors. Reversions to the original state of anergy are few among the members of this highly susceptible group. Conversion of natural reactors to the anergic state have occurred but are few. The morbidity, even in this limited observation, was lower than the natural reactor group; this fact has no definite significance.

The Treatment of Tuberculosis in Leprosy Patients. A. L. Relvich. Leprosy Rev. **25**:179-186 (Oct.) 1954 [London, England].

Relvich reports observations made in the Ossiomo Settlement, which became the center of leprosy control in Western Nigeria. With only two medical officers in charge of a fluctuating population of about 5,000 patients, and with no roentgenographic facilities, it has been impossible to diagnose early cases of tuberculosis. Only when a patient had been losing weight at an abnormal rate or had a constant rise in temperature or persistent cough was his sputum tested for acid fast bacilli. If tuberculosis was diagnosed, the patient was segregated in an isolation ward. He continued receiving the antileprosy treatment, and, in addition, a diet rich in proteins and vitamin preparations. In the five years between 1947 and 1951, pulmonary tuberculosis was diagnosed in 50 patients, of whom 45 have died. Sulfone treatment was introduced gradually in 1950 and early in 1951, but there has been no appreciable improvement as far as tuberculosis is concerned. Improvement came with the introduction in January, 1952, of thiosemicarbazone for patients with tuberculosis. Out of 16 patients who received that treatment until September, 1953, only 3 have died. In September, 1953, patients with tuberculosis of lungs and lymphatic glands were treated with 1 gm. of streptomycin on alternate days and 100 mg. of isoniazid twice daily. In two to three months the sputum of 14 out of 16 was rendered free of acid-fast bacilli, and the tuberculosis of cervical lymph nodes in the only patient who had this form has completely regressed. In two patients whose sputum was not cleared of the bacilli in four to five months, therapy has been changed from streptomycin to *p*-aminosalicylic acid and the sputum of one of the patients became free of bacilli in a month. Only one patient continued to discharge bacilli after nine months of treatment, but the treatment saved her life. The weight of all patients increased, and there has been noticeable subjective improvement. No appreciable improvement in the leprotic condition of the patients was observed. Treatment with isoniazid and streptomycin or *p*-aminosalicylic acid is recommended for leprosy patients with tuberculosis, but, because of the doubtful action of these drugs on the leprotic condition, this treatment should be combined with sulfones or thiosemicarbazone.

Skin Reaction with BCG. L. Sayé. Med. clín. **23**:279-282 (Oct.) 1954 (In Spanish) [Barcelona, Spain].

The author investigated whether virulent infection in BCG vaccinated persons could be detected by the BCG skin reaction. One hundred one persons with virulent infection and 103 BCG vaccinated persons free from tuberculous infection were tested. The emulsion containing 10 cg. of live BCG per cubic centimeter was applied to a scratch of from 0.5 to 1 cm. on the deltoid region. A control scratch and an other scratch were made through a drop of the special BCG emulsion. The tests were read 24 to 48 hours later. Three different types of reaction were observed: (1) the tuberculin type, (2) the tuberculin-desquamative, and (3) the abortive-suppurative. The tuberculin type manifested itself by minimal edema and an area of erythema with a diameter of 1 to 3 mm. over the scarification. The tuberculin-desquamative type exhibited a marked edema and erythema. The diameter of the area of erythema was 5 to 6 mm. A crust was formed over the scarification in six or eight days and detached itself from the skin in one to three weeks. The abortive-suppurative type was the earliest to appear and the most acute. There appeared an area of infiltration and erythema that reached a diameter of 6 to 8 mm. The line of scarification suppurated or small suppurating nodules developed over the scarification. The reaction subsided in 8 or 10 days with the formation of a typical crust. The duration of the reaction was different in the various types. In BCG vaccinated persons the tuberculin type was identifiable for two or three months, whereas the reactions of the other two types lasted longer. The reaction was harmless and was not complicated by regional adenopathy or unpleasant symptoms. In the group of 101 persons with virulent infection, the tuberculin type of reaction predominated in patients with either latent or healed tuberculosis and in those with negative or attenuated forms of allergy. The other two types of reaction predominated in cases of active tuberculosis and in those with positive allergy. In the group of 103 BCG vaccinated patients without tuberculosis, reactions of the tuberculin type were constantly observed in persons with negative or attenuated forms of allergy and almost constantly in persons with positive allergy. The author concludes that the skin reaction with live BCG is of value in detection of virulent infection in BCG vaccinated persons, since the tuberculin type shows absence of virulent infection, whereas the desquamative and abortive suppurative types show presence of the infection.

Pathogenesis of Capillary Damage in Diabetes Mellitus. G. Stärck. Schweiz. med. Wchnschr. **84**:1440-1445 (Dec. 25) 1954 (In German) [Basel, Switzerland].

Of 1,352 patients with diabetes mellitus who were studied at the First Medical Clinic of the General Hospital Langenhorn in Hamburg, Germany, 850 were women and 502 were men. Of the 502 men, 344 were free of capillary damage and 158 (31.5%) showed capillary damage; 530 of the 850 women were free of capillary damage and 320 (37.6%) showed capillary damage. Stärck believes that the capillary damage in patients with diabetes mellitus may be elicited by an antigen-antibody reaction that results from the occurrence of specific intermediary products of diabetic metabolism. Independent of the severity of the diabetes mellitus and of the required amount of insulin, these intermediary processes, which occur in every patient with diabetes mellitus, cause an accumulation of metabolic products that may develop an antigenic character depending on the state of immunity and allergy that prevails in the individual patient. The preliminary stages that precede the clinically manifest acidosis are of particular importance. The body reacts under certain conditions with a production of antibodies. Precipitation takes place on the capillary system. The adrenal cortex plays an important part as a mediator. This concept explains why capillary damage may occur in patients with mild and even with latent diabetes mellitus. Clinical detection of the disturbance may be possible only after prolonged duration of diabetes, although abnormal processes may occur quite early. Age and sex of the patient, body weight, hypertension, severity of diabetes, insulin requirements, and blood cholesterol level are not significant. Serum protein changes revealed by electrophoretic studies and the diffuse capillary damage are not the cause but are secondary phenomena of the diabetic disturbance of metabolism. The author considers it indispensable from the therapeutic point of view that the patient be placed on an optimal high protein and low fat diet. Although restoration of blood sugar level to normal and absence of sugar in the urine should be the aim, it is of

primary importance to prevent the occurrence of acidosis or shock. Removal of foci should be carried out in order to prevent metabolic derangement. Administration of female or male sex hormones seems to exert a favorable influence on the capillary damage. Future studies will show whether the demonstration of autoantibodies, disappearance of complement titer, and daily curves of the acetone level in the blood may contribute to the elucidation of the causation of the capillary damage.

Effect of Vitamin B_{12} and Folic Acid in the Treatment of Viral Hepatitis. R. E. Campbell and F. W. Pruitt. Am. J. M. Sc. **229**:8-15 (Jan.) 1955 [Philadelphia].

The studies reported were made on United Nations military personnel admitted to the U. S. Army Hepatitis Center in Japan between July 1, 1950, and July 31, 1951. The patients were given a diet of 150 gm. of protein, 350 gm. of carbohydrate, and 100 gm. of fat. In addition, 8 oz. (249 gm.) of high protein milk formula were given after each meal and again at bedtime. The total caloric intake was 4,000 calories. The patients' trays were checked after each meal and the caloric value of the consumed food estimated. Ten per cent glucose in water by vein, or high protein milk formula by mouth, was given in lieu of the food not eaten. Bed rest was required of all patients, with one bathroom privilege daily. In addition to this regimen, one group of 44 patients received 30 mcg. of vitamin B_{12} by intramuscular injection every other day for the first 10 days of hospitalization and 5 mg. of folic acid by mouth three times daily for the first 10 days. The selection of controls was made on the basis of the maximum total serum bilirubin values attained during the clinical course. Unpublished data had revealed that the height of the total serum bilirubin is the only factor in the series that correlates with length of illness. Control patients were selected from a group receiving conventional hepatitis treatment. It was found that the patients receiving vitamin B_{12} and folic acid had a more rapid return of normal appetite. The total serum bilirubin values of the patients belonging to the experimental group were normal after the 11th week, whereas 18 weeks were required by the control group. The bromsulfalein values of the experimental group all became normal by the 11th week, whereas 17 weeks were required by the control group. The mean duration of illness of the experimental group was 47.5 days, as compared to 57.2 for the control group. The difference was most marked when the total serum bilirubin level was in excess of 15 mg. per 100 cc. of serum (17.2 days) but was appreciable (approximately 10 days) in those groups of persons in whom the total serum bilirubin was 5 to 10 mg. Experimental work links vitamin B_{12} and folic acid to nucleoprotein synthesis, choline oxidase, and coenzyme A systems.

Surprises in Punch Biopsy of the Liver. E. Benhamou, B. Ferrand and J.-C. Chiche. Presse méd. **62**:1778-1780 (Dec. 25) 1954 (In French) [Paris, France].

In performing over 500 punch biopsies of the liver, the authors have observed no accidents. They have on occasion found lesions that yielded an unsuspected, surprising diagnosis. These instances are described and divided into four categories: infectious and parasitic diseases, blood diseases, neoplastic or pseudoneoplastic hepatomegaly, and certain visceral affections. Under the first heading, it is mentioned that, in several relapse cases of malaria due to Plasmodium falciparum, small areas of cell disintegration were found in the liver, somewhat resembling those seen in viral hepatitis, although it had been thought that such lesions were rare. The histological picture seen in two patients with pernicious malaria, one of whom was jaundiced, was surprisingly unimposing, that is, the lesions were mild. Punch biopsy enabled a correct diagnosis of tuberculosis to be made in one instance, and, in another, a diagnosis of septicemia due to Bacillus funduliformis. Evidence of hepatic involvement in a patient with leprosy was revealed by punch biopsy in the total absence of symptoms relative to the liver. In the second category, a case is cited in which steatotic and cirrhotic lesions resembling those of Laennec's cirrhosis were found in a patient with malignant reticulosis. A hematological diagnosis of subacute erythroleukosis was confirmed by the biopsy. Three cases are cited in the third category. The first occurred in a patient with gastric cancer whose hepatic enlargement and induration were assumed to be metastatic but were proved at punch biopsy to be due to alcoholic cirrhosis. Another patient was suspected of having carcinoma of the liver, but the biopsy revealed fatty degeneration and a theretofore concealed history of alcoholic overindulgence was elicited from her. In the third instance, the patient was suspected of having a hepatic neoplasm, which was in fact the case, but punch biopsy showed the lesion to be a highly atypical epithelioma resembling a pulmonary small cell epithelioma; and in fact the patient did have recurrent attacks of pleurisy. Four patients mentioned under the fourth heading had cured cases of tuberculosis; in them punch biopsy of the liver showed latent amylosis. One patient with lepromatous leprosy and pulmonary tuberculosis was found to have hepatic amylosis and massive steatosis. Sometimes punch biopsy reveals a clinically asymptomatic hepatic amylosis that seems to be primary; one such case is described. Several cases of moderate hepatic steatosis were found among patients with lipoid nephrosis. In one patient, who had recently recovered from an episode of hepatitis with jaundice but had persistent hepatomegaly, punch biopsy showed posticteric cirrhosis, with considerable steatosis. Thanks to this procedure, suitable therapy was instituted and the prognosis much improved because of an early diagnosis.

Irreparable Changes of the Spinal Cord After Pellagra. W. E. F. Winckel. Docum. med. geog. et trop. **6**:296-302 (Dec.) 1954 [Amsterdam, Netherlands].

The patient whose case is reported had been a prisoner of war in Macassar (Celebes) in 1944. After a period of diarrhea he began to suffer from perlèche (a form of chronic ulceration of the commissures of the lips), sore and red tongue, impaired eyesight, and poor memory. He also had dermatitis and was considered to have typical pellagra. In the beginning of 1945 he developed tingling in the feet and later on in the hands. His tongue felt swollen. Walking gradually became difficult. Later he sustained spontaneous fractures of the femur, and he had an attack of meningitis, which he survived. The following year, hands and legs were stiff, and there was loss of sensation and tingling in hands and feet, also loss of muscular power of the extremities, and a swollen feeling in the lips, gums, and tongue. The patient died in shock, of subacute bacterial endocarditis and bronchopneumonia after he had been in hospital for about six months. The severe neurological complications of pellagra, resulting from anomalies of the dorsal funiculus, had proved irreparable. Examination of the lumbar portion of the spinal cord revealed disintegration of the neurofibrils and degeneration of the myelin sheaths in the dorsal funiculus, with the exception of the dorsomarginal zone. There was marked isomorphous gliosis of the macroglia.

Adult Agammaglobulinemia. R. L. Wall and S. Saslaw. A. M. A. Arch. Int. Med. **95**:33-36 (Jan.) 1955 [Chicago].

Agammaglobulinemia apparently occurs in adults as well as in children. This report is concerned with two men. The first patient had a number of congenital deformities (cleft palate, hip dislocation, deformities of legs and feet) and had repeated attacks of pneumonia and an attack of erysipelas. With the history of multiple infections, repeated electrophoretic studies of this patient's plasma, during his hospital stay and subsequently, revealed an absence of gamma globulin. Immunologic studies demonstrated that this patient did not form any antibodies in response to inoculations with triple typhoid, influenza, and mumps vaccines. Histoplasmin, tuberculin, and toxoplasmin skin tests were negative. The patient had a positive Schick test and negative heterophile, cold agglutinin, and antistreptolysin titers. The second patient had a sprue-like syndrome, with multiple other infections. One of the authors (Wall) was impressed by the low serum globulin and repeated infections, and, when he performed an electrophoresis on this patient's serum, it was evident that the patient lacked gamma globulin. The patient showed no antibody response to typhoid-paratyphoid vaccine. The authors feel that the repeated infections in the two patients could be attributed to the deficiency of gamma globulin and concomitant poor antibody response. Whether this

syndrome in both patients represents a congenital or an acquired defect in gamma globulin synthesis is difficult to ascertain. It is tempting to suggest that the syndrome was congenital in the patient with the multiple congenital defects.

Scleroderma: Pulmonary and Skin Studies Before and After Treatment with Cortisone. A. Salomon, B. Appel, E. F. Dougherty and others. A. M. A. Arch. Int. Med. **95**:103-111 (Jan.) 1955 [Chicago].

Generalized scleroderma is recognized as a disseminated disease that may involve not only the skin but many other organs. It is usually a chronic illness with a gradual downhill progression. The scarcity of pulmonary function studies in patients with scleroderma who were being treated with corticotropin or cortisone prompted Salomon and associates to report observations on the effect of cortisone in three patients with generalized scleroderma who had involvement of the lungs. Pulmonary function studies, including lung volume measurements, ventilation studies, and determinations of arterial blood gases, were made before and after treatment with cortisone. Care was taken to exclude the presence of a complicating infection, especially tuberculosis, prior to starting treatment. Cortisone by mouth was given for 35 days to each patient, with a dose of 300 mg. for 3 days, followed by 200 mg. for 5 days, and 100 mg. daily for 27 days. One gram of oxytetracycline (Terramycin) and 1 gm. of potassium chloride were given daily, and a low-salt diet was maintained during treatment. The three patients were women, ranging in age from 32 to 54 years. Objective and subjective improvement of varying degrees occurred in all patients. The skin lesions appeared to be more responsive than the visceral ones. Improvement of the dermatological manifestations was temporary, and relapse occurred in all three patients four to six months after therapy had been terminated. Pulmonary function was not significantly altered by treatment. No acute exacerbation of the disease occurred in these patients as a result of cortisone therapy. One patient, in whom a 35-day course of cortisone treatment was started in the fifth month of pregnancy, was delivered of a healthy infant. There was no obvious ill-effect on either mother or child.

Clinical Syndromes Associated with Hypernatremia. H. M. Schoolman, A. Dubin and W. S. Hoffman. A. M. A. Arch. Int. Med. **95**:15-23 (Jan.) 1955 [Chicago].

Schoolman and co-workers feel that, although cases of hypernatremia (serum sodium levels above 150 mEq. per liter) were reported by Allott in 1939, and despite numerous subsequent reports about this condition, the frequency of occurrence of hypernatremia is not sufficiently appreciated. The authors observed over 100 cases of hypernatremia during the last four years. With few exceptions the cases of hypernatremia occurred in three categories of patients: in 15 children with primary desiccation, in 63 patients with injuries of the central nervous system, and in 9 patients with diabetic coma who had been treated only with insulin and isotonic solution of sodium chloride. The treatment of hypernatremia is the intravenous or oral administration of nonsaline fluids. Such treatment is usually successful except in cases of central nervous system injury severe enough to produce death.

Differentiation of Hyperparathyroidism and Milk-Alkali (Burnett) Syndrome. L. H. Kyle. New England J. Med. **251**:1035-1040 (Dec. 23) 1954 [Boston].

The most recent addition to the list of hypercalcemic disorders that may stimulate hyperparathyroidism is the syndrome of excessive intake of milk and absorbable alkali. This interesting condition, first clearly delineated by Burnett and his associates in 1949, is characterized especially by hypercalcemia without hypercalciuria. In the five years since the original report, 10 additional cases have been described. The two cases reported in this paper illustrate the difficulties in clear-cut separation of hyperparathyroidism and the milk-alkali syndrome. Although both patients demonstrated all the criteria for the diagnosis of dietary hypercalcemia, one was shown to have a parathyroid adenoma. The features that suggest the presence of the milk-alkali syndrome include a history of prolonged and excessive intake of milk and alkali; hypercalcemia without increased urinary calcium excretion; depression of serum phosphorus; skeletal involvement; renal failure with azotemia; calcinosis; mild alkalosis; and improvement on diet low in calcium and absorbable alkali. The presence of the milk-alkali syndrome is suggested by the combination of azotemia and alkalosis. Although the response to dietary correction is most helpful in diagnosis, the presence of irreversible renal failure may necessitate histological examination of the parathyroid tissue. Both band keratopathy and pruritus occur in other hypercalcemic disorders but appear to be especially frequent in patients who ingest large amounts of milk and alkali. Available data indicate that this syndrome occurs because of renal impairment secondary to the alkalosis, combined with increased intake and decreased excretion of calcium.

Results of Studies on Biopsy Material and of Gastroscopy on the Gastric Mucosa in Presence of Duodenal Ulcer. N. Henning, K. Heinkel and K. Elster. Klin. Wchnschr. **32**:1088-1092 (Dec. 1) 1954 (In German) [Berlin, Germany].

Henning and associates cite investigators who concerned themselves with the theory that inflammation plays a part in the development of peptic ulcer and then show that in recent years this theory of an inflammatory pathogenesis has been challenged. They decided to search for evidence of diffuse inflammation in stomachs of 34 patients with peptic ulceration. Thirty of these patients had roentgenologic evidence of duodenal changes, a florid ulcer being present in 22 and a deformed duodenal bulb in 8. The remaining four patients had a history of duodenal ulcer. All 34 patients were receiving clinical treatment for gastric disturbances. The acid secretion of the stomach was ascertained by fractional aspiration after a caffeine test drink. Gastroscopy was done with a flexible gastroscope. Suction biopsy served to obtain a lentil-sized piece of gastric mucosa. The biopsy material was taken after gastroscopic control from the anterior wall of the stomach in the lower third of the fundus. The biopsy specimen of gastric mucosa was fixed in 10% solution of formaldehyde within two minutes of its withdrawal. In making sections care was taken that the direction of the knife was rectangular to the surface of the mucosa. The results of these studies indicated that neither during the acute nor in the later stage of peptic ulceration are essential changes demonstrable in the gastric mucosa. Duration and severity as well as frequency of relapses of typical duodenal ulceration are without influence on the gastric mucosa. The authors feel that the demonstration of a normal or increased acid production and of a continuous, even nocturnal, supersecretion is in agreement with the histological picture of an intact gastric mucosa.

Cortisone in the Treatment of Chronic Hereditary Edema (Milroy's Disease): Case Report. S. J. Dencker and I. Gottfries. Acta med. scandinav. **150**:277-280 (No. 4) 1954 (In English) [Stockholm, Sweden].

A case of the hereditary type of chronic edema (Milroy's disease) is described in a 22-year-old woman. The patient's mother, a 43-year-old woman, had elephantiasis-like edema of the feet and lower legs; an aunt had had severe edema of the lower legs; and the patient's younger sister had slight enlargement of one of her ankles. The patient's feet had probably been slightly edematous throughout childhood, but the disease did not make its clinical appearance until puberty. The legs were involved and occasionally the upper extremities. Premenstrual accentuation of the symptoms suggested endocrine involvement. The patient was allergic and an allergic component cannot be excluded. There was no clue to any local cause. The disorder apparently was not caused by cardiac or renal disease, nor were any signs of disturbed protein metabolism demonstrable. The patient did not respond to treatment with hyaluronidase, which was practiced for one week. Cortisone then was administered parenterally for one month, and the total dose given was 3 gm. Despite the fact that the patient was in the premenstrual phase at the beginning of the cortisone therapy, the edema promptly disappeared. The pain in the legs subsided. On withdrawal of cortisone, pain and edema gradually reappeared. This suggests a specific effect of cortisone rather than a spontaneous remission. The favorable response in this case may be ascribed to the fact that the patient received treatment before the development of indurative changes.

Acute Intermittent Porphyria: Report of Five Cases and Review of the Literature. M. Markovitz. Ann. Int. Med. **41**:1170-1188 (Dec.) 1954 [Lancaster, Pa.].

The author saw five women with acute intermittent porphyria. These cases and 64 others reported in the literature fulfilled the following criteria: porphobilinogen and/or uroporphyrin were found in the urine, photosensitivity was not present, and symptoms were present. Of the 69 patients, 42 were women and 27 were men. The three main types of symptoms in acute intermittent porphyria are abdominal pain, peripheral neuropathy, and mental or psychic changes. The initial complaint of 49 patients was abdominal pain. This pain simulated acute surgical emergency, and 48 operations were performed in 32 patients of the series, the majority being unnecessary. Constipation was a symptom in about 50% of cases. Motor symptoms ranging from weakness to quadriplegia were reported in over 75% of them. Mental disturbances included irritability, restlessness, confusion, delirium, hallucinations, and epileptiform seizures. In 18 patients a diagnosis of hysteria, schizophrenia, depression, or paranoia was made. Vocal changes were noted in 26. Half of the patients in the series had blood pressures of 150/100 mm. Hg or more, and an equal number had tachycardia. About 70% had dark urine. Leukocytosis was present in 24. Definite or suggestive evidence of a family history of porphyria was found in 11 instances. Diagnosis of the disease is not difficult to make, but the index of suspicion must be high. The use of corticotropin or cortisone has been reported in six patients with porphyria; it appears to be of value, but the evidence is inconclusive. Patients should be warned against the use of barbiturates, sulfonamides, and heavy metal medication. Acute intermittent porphyria has a bad prognosis; in the present series of 69 patients, the over-all mortality rate was 58%. The greatest mortality, 63%, was among those patients with cranial nerve involvement. Only one of the 15 patients with no peripheral or cranial nerve involvement was dead at the time of the report.

The Effect of the Previous Diet on Glucose Tolerance Tests. E. M. Irving and I. Wang. Glasgow M. J. **35**:275-278 (Nov.) 1954 [Glasgow, Scotland].

Irving and Wang point out that after observations reported by Himsworth in 1933 it has been widely accepted that in the normal person a low carbohydrate diet can result in an abnormal glucose tolerance test. In order to eliminate any such misleading results, Conn in 1940 suggested that for three days before any glucose tolerance test the patient should take a diet containing not less than 300 gm. carbohydrate. The present authors found that in many patients a diet containing 300 gm. of carbohydrate is far in excess of normal requirements and proves nauseating. They investigated whether the diet containing 300 gm. of carbohydrate was necessary in a person whose diet had been sufficient to maintain adequate nutrition. A diet containing 100 gm. carbohydrate daily was chosen as being probably below the daily consumption of the hospital patient maintaining adequate nutrition. The effect of this diet on the sugar tolerance of 12 normal persons was compared with that of a diet containing 300 gm. carbohydrate daily. After the low carbohydrate diet, no values were obtained that approximated a diabetic curve, but it was noted that in two cases an oxyhyperglycemic curve was obtained. It is concluded that there is no necessity for augmenting the normal diet of an adequately nourished patient before the performance of a glucose tolerance test.

The Submersion Syndrome. M. Saline and G. L. Baum. Ann. Int. Med. **41**:1134-1138 (Dec.) 1954 [Lancaster, Pa.].

The clinical records of 26 persons surviving submersion are reviewed. Chest roentgenograms were made in 11 instances; five of them showed evidence of pulmonary congestion or edema. Nineteen patients had clinical evidence of pulmonary congestion and edema. Sixteen were dyspneic and cyanotic. Leukocytosis with shift to the left was present in 22 patients. Neurological disturbances occurred in 13, shock in 8, moderate fever in 7, and gastrointestinal symptoms in 5. The average duration of hospital stay, exclusive of one patient in whom acute myocardial infarction developed, was 2.5 days. One case is described in detail. The clinical, radiographic, and hematological changes described are related solely to the effects of asphyxia and not to those of aspiration. Aspiration pneumonia can be eliminated because of the short duration, lack of significant pyrexia (no temperature above 101 F was noted), and transitory pulmonary manifestations. The symptoms of the submersion syndrome are dependent on the degree of hypoxia. It is felt that the elevation of the leukocyte count is a nonspecific effect of stress, with the production of a neutrophilia associated with a lymphopenia.

SURGERY

Arteriosclerotic Occlusion of the Terminal Aorta and Common Iliac Arteries Treated by Thromboendarterectomy: An Evaluation of the Procedure Based on the Results Obtained in Twenty Cases. H. M. Coelho, F. H. Leeds and N. E. Freeman. Surgery **37**:105-114 (Jan.) 1955 [St. Louis].

Of 16 men between the ages of 45 and 66 years and 4 women between the ages of 51 and 58 with thrombosis of the terminal aorta and common iliac arteries who were subjected to thromboendarterectomy, 10 had Leriche's syndrome (thrombotic obliteration of the aortic bifurcation), 7 had complete occlusion of one common iliac artery with stenosis of the terminal aorta, one had a partial aortic occlusion, and 2 had an aortic occlusion just below the inferior mesenteric artery but with patent iliac arteries. Aortography by the lumbar percutaneous method was performed in all patients except one, who had a retrograde left carotid arteriogram with Valsalva maneuver. Forty cubic centimeters of 70% concentrated iodopyracet (Diodrast) or 25 cc. of sodium acetrizoate (Urokon sodium) in the same concentration was used after previous sensitivity tests, conjunctival and sublingual for the former and intravenous for the latter solution. Six to eight exposures were made with a time interval of approximately one second, with the use of a fast cassette changer. This series of films permitted a clear visualization of the proximal and distal parts of the occlusion and a good study of the collateral circulation. The presence of patent distal arteries was considered essential for the success of the operation, the technique of which is described in detail. An excellent clinical result was obtained in 18 of the 20 patients. They have all recovered their ability to walk without claudication. Thirteen of the 14 men noted a return of their ability to maintain an erection, although they have been unable to ejaculate. This fact may be explained by the presacral neurectomy necessarily performed in the course of the dissection of the terminal aorta. Peripheral pulses returned in all but two patients. One death occurred from hemorrhage, presumably caused by overdosage of heparin. In one patient thrombosis recurred at the operative site immediately after the operation. The fact that regional heparinization was not used in this patient may be significant. Cerebral thrombosis, which developed in one patient, was the only complication of arteriosclerosis observed so far in the 19 patients who have been followed for from one to 39 months and who, with one exception, have fully recovered from the impairment of circulation to the lower extremities and pelvis. The low morbidity and mortality make thromboendarterectomy useful in selected patients with circulatory impairment caused by occlusion or stenosis of the aorta and common iliac arteries.

A Critical Evaluation of Lumbar Sympathectomy for Peripheral Arteriosclerotic Vascular Disease. R. E. L. Berry, C. T. Flotte and F. A. Coller. Surgery **37**:115-129 (Jan.) 1955 [St. Louis].

Three hundred ninety-seven lumbar sympathectomies were performed for arteriosclerosis obliterans of the lower extremities in 275 patients at the University of Michigan Hospital between 1945 and 1952. A minimum 12 months' follow-up was obtained in 271 patients (98%). Most of the patients were between the ages of 50 and 70 years, and 11 patients were over 75 years of age. Of the 275 patients, 41 had intermittent claudication only, 24 had intermittent mild or moderate rest pain with or without intermittent claudication, 43 had severe constant rest pain with or without intermittent claudication, 165 had tissue necrosis, and 2 were asymptomatic. All sympathectomies were performed through transverse incisions immediately lateral to the umbilicus with extraperitoneal dissection. The sympathetic chain was removed between the second lumbar vertebra

and the bifurcation of the aorta. Of the 41 patients with intermittent claudication only, 20 obtained good results and 15 obtained no benefit but did not require amputation; amputation was necessary in 4, and 2 died in the hospital. Seven additional patients died after leaving the hospital. There would appear to be some correlation between severity of claudication and result, since good results were obtained in 6 of 10 patients with mild claudication, 13 of 25 with moderate claudication, and only 1 of 5 with severe claudication. Of the 24 patients with mild ischemic pain, 10 obtained good results, 7 obtained no benefit, and amputations were performed on 7, none obtaining any help before the amputation. Of the 43 patients with severe pain, 17 obtained good results, and only 3 of these died; 12 had little benefit from the operation but did not require amputation, and 11 of these died, usually within one year after the sympathectomy. Eleven amputations were necessary in 44 extremities in which sympathectomy had been done; three patients died in the hospital after the operation. Of the 165 patients with tissue necrosis, 47 (28%) obtained good results, 21 (13%) had poor results but did not require amputation, 97 amputations were performed in 86 patients (a 55% amputation rate), and 69 (42%) died. Sympathectomy was performed prophylactically in two asymptomatic patients with a previous supracondylar amputation in an attempt to improve the circulation of the remaining leg. Potential long-term beneficial effects could not be observed, as both patients died within two years. Thus, of the total of 275 patients operated on, 94 (34%) obtained good results, 55 (20%) had poor results but did not require amputation, and 119 (41%) required amputation. Of all patients operated on, 108 (39%) are now dead; the average survival time was 25 months; one-third lived less than one year. Comparative analysis of diabetic and nondiabetic patients with ulceration or gangrene revealed the results to be essentially the same. The following types of patients have a minimum chance of obtaining a good result from lumbar sympathectomy, although the operation is not absolutely contraindicated: (1) elderly diabetic persons with clinical evidence of arteriosclerotic involvement of other organs or elevated systolic blood pressure; (2) patients with severe atrophy of the soft parts of the leg with evidence of pronounced capillary anoxia; (3) patients with severe pain involving the foot or lower third of the leg with absent popliteal pulses; (4) patients with a rapidly progressing process with widespread arterial involvement; (5) patients over 60 years of age with gangrene or ulceration involving the foot and with severe pain and obliteration of the popliteal pulses. Of the 397 sympathectomies, 165 were unilateral and 116 bilateral. Evidence is presented supporting the desirability of bilateral operation, provided that it is compatible with the patient's general condition.

Lower Thoracic and Lumbar Sympathectomy for Arteriosclerotic Obliterative Disease of the Lower Aorta or the Iliac Arteries. K. S. Grimson, G. J. D'Angelo, A. A. Zavaleta and A. P. Hustead. Surgery **37**:146-155 (Jan.) 1955 [St. Louis].

Excision of the lower thoracic ganglions, up to or including the ninth thoracic, and all of the lumbar sympathetic ganglions was carried out in 19 patients with unilateral or bilateral obstruction of the terminal aorta or iliac arteries and with viable limbs. Of the 19 patients, 8 had unilateral lower thoracic and lumbar sympathectomy, 5 had a high sympathectomy on one side and a conventional lumbar sympathectomy for the opposite limb, and 6 had bilateral high sympathectomy. Follow-up varied from 6 to 64 months. Five additional patients with obstruction of the terminal aorta or the iliac arteries or both differed from the preceding 19 patients, since pronounced resting pain, pronounced patchy cyanosis, and pallor of one or both feet or limbs and other evidences of serious ischemia suggested impending gangrene; among other operative procedures, thromboendarterectomy was performed in 4 of these. None of the 19 patients died, and only one patient required amputation of one limb four years after sympathectomy. All the patients were satisfied with the result of the operation for each limb. Each had a warm foot on the operated side, and all were carrying on relatively normal occupations, without a significant handicap. Oscillometric readings remained low or absent. Persistence of claudication of the leg in which sympathectomy was done was accepted as a necessary and minor inconvenience. Results obtained indicate that high segmental obstruction is less serious than the more common atherosclerosis involving arteries lower in the leg. Results of high sympathectomy for high segmental obstruction seem better than the fairly good results of conventional lumbar sympathectomy as commonly used for more peripheral arterial obstruction. Results of either operation are best as judged by satisfaction of the patient and warmth of limb, poorest as judged by incidence of relief from claudication or improvement of oscillometric readings. Comparison of the results of high sympathectomy with those of arterial grafting, thromboendarterectomy, or the conventional lumbar sympathectomy after five years or longer should permit a formulation of indications for each operation. At present, lower thoracic and lumbar sympathectomy continues as the authors' preference for most patients meeting indications for surgical intervention and yet having no symptoms or findings of impending gangrene. As indicated by results of treatment in the five patients with impending gangrene, no operation or combination of operations was entirely successful. A direct surgical approach into the arteries seems best indicated in this group of patients. Sympathectomy alone does not seem indicated as a primary operation. Instead, it may be used as an adjunct to treatment.

Method of Blood Vessel Anastomosis by Means of Metal Clips: Experimental Study. P. B. Samuels. A. M. A. Arch. Surg. **70**: 29-38 (Jan.) 1955 [Chicago].

Samuels describes a method of blood vessel anastomosis by means of V-shaped clips, with a circle of spikes at either end, which grip the vessel wall and effect coaptation when compressed. The silver clips used initially proved unsatisfactory owing to lack of rigidity, dull spikes, and local reaction of the tissues. At present the clips are made from stainless steel sheets, No. 302, cold-rolled, full temper, 0.005 in. thick. The dimensions of the present design make them satisfactory for use in dog aortas. The clips are handmade. The clips are presently being applied with ordinary straight and curved hemostats. Mongrel dogs were used in experiments with these clips. The thoracic aorta was selected for use in the majority of operations because of its friability, strong tendency to retract on section, brief period of safe occlusion, and the swift and certain outcome of a faulty anastomosis. Tables record the data on 6 dogs subjected to longitudinal arteriotomy and intimectomy, on 10 dogs in which single transection and reanastomosis was done on the aorta (the thoracic in 9, and the abdominal in one case), and on 18 dogs in which double transection and reanastomosis was done. Of the six deaths in this last group of 18 dogs, one occurred on the table as a result of technical error. The remaining deaths occurred postoperatively. Two dogs are believed to have died from an overdose of anesthetic. The occlusion times in these animals were 15 and 16 minutes. One dog died five days postoperatively as a result of heart failure with pleural effusion. Another dog died after three days of unknown causes. In the remaining dog a chest wall infection developed, and the animal died 14 days postoperatively. In all postoperative deaths, the anastomoses were intact and the lumens clear. Two animals were killed on the 38th and 23d days postoperatively. The remaining dogs have survived without incident. The average occlusion time was 15 minutes for this series. Microscopic sections at various stages of the healing process allow the sequence of events to be reconstructed as follows. Immediately postoperatively the cleft in the intimal surface is filled in with fibrin. The exudate from the surrounding area coats the external surface of the vessel. The edges held by the clips begin within two to three days to show signs of pressure necrosis (thinning of elastic fiber and smooth muscle bundles—pallid staining and pyknosis of nuclei). Within three to four days the fibrinous coats on the internal and external surfaces are invaded by a vascular granulation tissue, which is converted gradually over a two-week period into fibrous tissue. The main bulk of the tissue binding the vessel together appears on its external surface. Endothelial cells cover the granulation tissue-fibrin mass within three to four days, but complete reconstitution of the intima takes three to four months. Medial

healing is seen in the completed stage as a thin fibrous band interrupting medial continuity. The author feels that, until confidence in this method grows with clinical trial, it can be regarded as a rapid method of reestablishing blood flow. After release of occlusion clamps, interrupted sutures may be placed at leisure between the clips to reinforce the anastomosis. It is hoped that the clips may ultimately be produced in three sizes suitable, respectively, to arteries such as aorta, carotid and femoral, popliteal, and brachial.

Failure of Polyethylene Wrapping in Treatment of Aortic Aneurysms. M. E. De Bakey, O. Creech Jr., D. A. Cooley and B. Halpert. A. M. A. Arch. Surg. **70**:65-78 (Jan.) 1955 [Chicago].

Previous reports based on certain experimental studies and clinical observations suggested that the polyethylene wrapping procedure, with use of polyethylene film containing dicetyl phosphate, would produce a fibroblastic response that could be useful in the treatment of aortic aneurysms. Its efficacy, however, has not been well established clinically. The authors present the histories of eight patients with aneurysms of the abdominal aorta who had been treated earlier by polyethylene wrapping and in whom resection was done subsequently. The interval between the cellophane wrapping procedure and subsequent resection varied from 7 to 41 months. Varying degrees of symptomatic improvement occurred after the polyethylene wrapping procedure in most of these patients, and in a few this lasted for about a year. In all the patients, however, there was recurrence of symptoms and progressive increase in size of the aneurysms. This enlargement in the dimensions of the aneurysms varied from slightly less than a fourth to about twice the size at the initial operation. In some this took place slowly and gradually, while in others it seemed to develop rapidly. At the second operation a characteristic finding was a relatively minimal degree of fibrosis in the tissues immediately overlying the sheets of polyethylene. Indeed, it could often be observed glistening through the thin overlying posterior peritoneal layer. The impression was gained that the presence of the polyethylene actually facilitated mobilization of the aneurysm from the surrounding tissues. Morphological studies demonstrated that the fibroblastic reaction was both grossly and histologically inadequate to provide significant reinforcement. The conclusion is reached that it is unlikely that the reaction induced by the implanted polyethylene could have favorably altered the natural course of the aneurysm. There is reason to believe that the polyethylene wrapping procedure may have an unfavorable effect by its potential tendency to devitalize the sac.

Study of Basic Physiologic Changes Associated with Hypothermia. R. A. Deterling Jr., E. Nelson, S. Bhonslay and W. Howland. A. M. A. Arch. Surg. **70**:87-94 (Jan.) 1955 [Chicago].

The search for a method that would permit intracardiac surgery under direct vision has focused attention on induced hypothermia by surface cooling. However, the relatively high incidence of ventricular fibrillation and death in dogs at body temperatures below 28 C (84 F) poses a real hazard for practical application to clinical surgery. Furthermore, little is known of acid-base balance and metabolic behavior in mammals in the hypothermic state. Deterling and associates present studies that were designed to provide further information on the physiological effects of reduced body temperature. Thirty adult mongrel dogs were subjected to a reduction in body temperature to 21 to 18 C (70 to 66 F) over a period of 45 to 90 minutes. Muscle relaxants were administered when necessary to suppress shivering and respiratory efforts. The dogs were wrapped in rubber sheets and packed in ice until the desired lowering of body temperature was almost achieved. In general, a further reduction in rectal temperature of 3 to 5 degrees occurred after removal from the ice. The animals were divided into three groups on the basis of differences in the pattern of artificial respiration. It was found that a metabolic acidosis developed during hypothermia that was not reversed by warming. A fall in blood pH could be prevented by control of shivering and by hyperventilation. Ventricular fibrillation occurred in seven animals, in six of these below 23 C (74 F). This serious arrhythmia did not occur in animals in which the pH was consistently elevated. No significant alterations in results of blood chemistry studies or electrolytes were observed during hypothermia. Increase in venous clotting time was observed without change in prothrombin time. The blood pressure, pulse rate, and oxygen consumption were decreased with cooling in a consistent pattern.

Repair of Large Losses of Diaphragmatic Substance with Preserved Fascia Grafts: Experimental Study. G. Esposito, A. Infranzi and A. Riccio. Gior. ital. chir. **10**:804-816 (Oct.) 1954 (In Italian) [Naples, Italy].

A series of experiments on dogs proved that grafts of fascia or aponeurosis can be used to repair extensive losses of diaphragmatic substance. In a first group of dogs the grafts used were autoplastic and were secured during the repair operation; in another group the grafts had been preserved in a Phargan solution for from 5 to 15 days. This antihistamine solution proved to be a good medium for the preservation of the grafts, which maintained their physical properties and histological characteristics for about 15 days. Autoplastic, fresh grafts of aponeurosis are preferred in this operation, because the host defense reaction is less marked. The authors' results were good in all the dogs in which these grafts were used. When it is not possible to use autoplastic grafts, preserved homoplastic grafts are a good substitute. The one failure in one of the dogs in which these grafts were used was caused by empyema and not by the graft itself. At autopsy this appeared to "have taken" well. All the animals were killed at varying intervals seven days to five months after the operation. The macroscopic examination revealed a marked difference between the two groups of dogs. There were more and stronger adhesions in those in which homoplastic grafts were used, and the grafts were irregular with thin and less resistant zones alternating with more consistent zones. The consistency of the autoplastic grafts was uniform. Histologically, in the dogs in which autoplastic grafts were used the host reaction was less marked, the invasion of small cell elements slower, the connective tissue more or less unchanged, and the fibroblastic infiltration responsible for the coarctation of the graft less marked. In those in which homoplastic grafts were used there was instead a more rapid and more intense invasion of the connective tissue that resulted in a partial disappearance of the transplanted tissue and its transformation into fibrous tissue. Thus, fresh, autoplastic grafts of fascia or aponeurosis or, when these are not available, preserved homoplastic grafts of the same can be used to create a solid septum between the thoracic and the abdominal cavities. These types of grafts can be obtained, handled, and transplanted easily, and, in addition, they are of elastic tissue, which guarantees the static and functional purpose for which they are used.

NEUROLOGY & PSYCHIATRY

Recovery of Language Function After Left Temporal Lobectomy for Astrocytoma. J.-A. Chavany, B. Pertuiset, G. Lobel and D. Hagenmuller. Presse méd. **62**:1805-1807 (Dec. 25) 1954 (In French) [Paris, France].

The case of the right-handed patient with a left intratemporal tumor and no speech impairment is a problematic one; often in such cases neurosurgical intervention is put off for fear that the patient may be left completely aphasic. Such a case is here reported in detail. A 35-year-old French dredge-boat mechanic had neurological symptoms of two years' duration. He underwent left temporal lobectomy for an astrocytoma; during the entire excision the patient was made to speak, thereby insuring that no serious damage was done to this function. At the end of the procedure he could tell his name, count, and obey simple orders. Forty-eight hours later, he was remaining silent, communicating his wants by gestures, but he was capable of answering simple questions intelligently. Speech and writing reeducation was tedious, and the patient was often frustrated in his attempts to carry out what was asked of him, causing him to swear frequently. Nevertheless, gradual progress was evident. He was discharged after a 17-day hospital stay. When seen 45 days after operation, he could carry on a conversation but had

trouble remembering the names of certain objects. A year and a half later he was virtually normal. A striking feature of this case, one of the two disorders that remained permanent with the patient, was his inability to define abstract expressions; he was always forced to resort to concrete terms to explain himself, e. g., "patriotism is a guy who loves his country." In addition, the patient had a tendency to forget proper names, which was a mild social handicap. It is maintained that an important factor in the good recovery of language function in this instance was the integrity of the remaining portion of the brain. Another favorable factor was the fact that the lesion was an astrocytoma, a tumor having slow development permitting displacement of the functional projections of the language function during the growth of the tumor.

Studies on Some Clinical Features of Poliomyelitis: I. The Relation of the Clinical Features in Bulbar Poliomyelitis to Tonsillectomy Status. R. V. Southcott. M. J. Australia **2**:845-852 (Nov. 27) 1954 [Sydney, Australia].

Southcott says that in 1952 he together with Top demonstrated a long range association between bulbar poliomyelitis and previous tonsillectomy. It was found that 85% to 90% of patients with bulbar poliomyelitis had previously undergone tonsillectomy and that the duration of the association was at least 9 to 10 years. In the 1947-1948 epidemic of poliomyelitis in South Australia, on which these studies were based, there were only four patients in whom tonsillectomy had not been done in a series of 39 with bulbar poliomyelitis. These four patients had a high incidence of "encephalitic" manifestations, using this term to include both patients showing evidence of cerebral damage and those with oculomotor lesions. Since this series of patients in whom tonsillectomy had not been done was small, the patients with bulbar poliomyelitis observed in South Australia during 1949-1950 were also investigated. Inquiry revealed that 14 of 30 had undergone tonsillectomy and 5 had not. In the other 11 the tonsillectomy status was not known. Thus, there was available for study a total of nine patients with bulbar poliomyelitis in whom tonsillectomy had not been done. There was a higher incidence of ophthalmoplegia in patients with bulbar poliomyelitis in whom tonsillectomy had not been done than in those in whom it had. This is so for abducens lesions. There is a suggestion that this is also so for oculomotor lesions, but in this latter case the figures available were too small for conclusions. The incidence of clinical lesions for other cranial motor nuclei was examined, but no differences were found between patients with bulbar lesions in whom tonsillectomy had or had not been done.

Studies on Some Clinical Features of Poliomyelitis: II. Interrelations Between the Clinical Features of Poliomyelitis, with Comments on Vomiting, Portal of Entry and Pathogenesis. R. V. Southcott. M. J. Australia **2**:885-891 (Dec. 4) 1954 [Sydney, Australia].

Southcott studied the relationships between encephalitic, bulbar, and spinal manifestations in patients with paralytic poliomyelitis in the South Australian epidemic of 1947-1948. There was a close association between encephalitic and bulbar manifestations. Some investigators extend the term "bulbar poliomyelitis" to signify what could more properly be called "brain stem poliomyelitis." He does not favor extending the term bulbar to include, for example, oculomotor lesions, as such a system of lumping divergent phenomena in one category would only confuse the relationships. When the term bulbar is used in the restricted sense that has been adopted in these studies, there is an association between oculomotor manifestations and bulbar manifestations. An analysis of incidence of symptoms and death in various clinical subgroups revealed the association between bulbar manifestations and death. In bulbar poliomyelitis there is a significantly higher incidence of vomiting than in nonbulbar poliomyelitis. It is suggested that this effect is due to lesions of the medullary vomiting center analogous to lesions of the medullary respiratory and circulatory centers in bulbar poliomyelitis. It is postulated that there are two mechanisms of vomiting in poliomyelitis. The first is central (medullary) vomiting, due to interference with the medullary vomiting center from local invasion with virus. This mechanism operates only in the bulbar cases. The second form is vomiting initiated from local effects within the gastrointestinal tract. This mechanism may operate in all forms of poliomyelitis, including nonparalytic, nonbulbar paralytic, and also bulbar. Studies were made on the time interval between onset of symptoms (earliest prodromal date) and the onset of headache and vomiting. There is a tendency for vomiting to occur earlier in the nonparalytic than in the paralytic cases. It was suggested earlier that in the subjects with bulbar poliomyelitis in whom tonsillectomy had been done (long before or recently) the virus gained entry from the tonsillar area along the motor nerve fibers to the nucleus ambiguus and from there to the neighboring medullary reticular areas. The medullary vomiting center is included in this mechanism, as well as the respiratory and circulatory centers. It is proposed that in the subjects with bulbar poliomyelitis in whom tonsillectomy has been done the virus spreads forwards from connections with the nucleus ambiguus along the brain stem to involve the oculomotor nuclei. That the pathogenesis differs between the patients in whom tonsillectomy has and has not been done is indicated by the higher incidence of abducens lesions in the patients with bulbar poliomyelitis in whom tonsillectomy has not been done.

Convulsion Dependence. H. Bourne. Lancet **2**:1193-1196 (Dec. 11) 1954 [London, England].

Bourne defines convulsion dependence as that condition in which the patient needs regular convulsions, induced or spontaneous, in order to maintain social adaptation. Convulsion dependence is observed only in psychoses. The frequency with which convulsions are required varies. Some patients require convulsions more than twice a week, others less than once a month. The convulsion dependence may be (1) transient, in which case the patient relapses unless electroconvulsion therapy is continued at an adequate dosage for a short period after apparent recovery; (2) it may be protracted, in which case electroconvulsion treatment is necessary for several weeks or months after recovery or improvement are apparently stabilized; or (3) it may be persistent (chronic), in which case the patient remains dependent on electroconvulsion treatment at regular intervals indefinitely. The author discusses the clinical features of transient, protracted, and persistent convulsion dependence on the basis of illustrative case histories. In the light of convulsion dependence, two main phases of convulsion therapy need to be recognized: (1) a dynamic phase, in which symptoms diminish or disappear; and (2) a static phase, in which relapse is likely unless the treatment is continued. It is because these fundamentals still lack general recognition that there is so much divergence of opinion over electroconvulsion treatment. For example, in early schizophrenia, in which transient or protracted convulsion dependence is common, poor results are obtained with the courses used in Britain and the mythical superiority of insulin is entrenched. Those recommending more extensive courses of electroconvulsion therapy obtain better results. The author feels that this may be due to the fact that the longer courses may cover the phase of convulsion dependence. In the management of the convulsion-dependent phase one rule is absolute: electroconvulsion treatment should never be stopped abruptly, no matter how well the patient seems. Relapse is probable if treatment is withdrawn so soon as remission, or an optimal level, is attained. Convulsion therapy cannot be mechanically prescribed ahead, and each course must be determined by individual differences and by day-to-day observation. Convulsion dependence has theoretical bearings as well. Its occurrence with certain diseases, such as schizophrenia, shows that these are responsive to convulsion therapy; conversely, its exclusive association with psychoses provides further reason for doubting its value in neuroses. Psychotic breakdown and recovery can be followed repeatedly in the convulsion-dependent subject, and the elusive prodromes of psychosis become identifiable.

GYNECOLOGY & OBSTETRICS

New Therapy for Prevention of Post-Operative Recurrences in Genital and Breast Cancer: Six-Year Study of Prophylactic Thyroid Treatment. A. A. Loeser. Brit. M. J. **2:**1380-1383 (Dec. 11) 1954 [London, England].

Loeser says that as early as 1938 he demonstrated the beneficial effect of male sex hormone on inoperable breast cancer and thought that he had found a means of preventing recurrence of breast cancer. Later he observed that prolonged treatment with one sex hormone involved the danger of completely blocking the anterior lobe of the pituitary. Necroptic studies had revealed that the anterior pituitary may shrink to a third of its normal size and may eventually deprive the body of the adrenotropic and thyrotropic hormones necessary for the maintenance of normal life. From 1950 on Loeser obtained much better results by combining the male hormone with thyroid hormone in the treatment of inoperable breast cancer. Loeser now advocates the use of thyroid hormone alone in the prevention of recurrence of breast and genital cancer after radical operation or x-ray treatment, because it supports normal cell metabolism. The records of life insurance companies show that more overweight persons acquire cancer than persons of normal weight. That a lack of thyroid hormone favors tumor development was proved by follow-up studies on 100 patients who had undergone partial thyroidectomy. Among these Loeser found seven with cancer (one of the cervix, six of the breast). Chronic mastitis (on an endocrine basis) developed in 32 of the remaining 93 women who had undergone thyroidectomy, and none of these 32 had ever received thyroid hormone. Among the then remaining 61 patients were 14 who had received thyroid hormone after thyroidectomy, and in only four could a chronic mastitis be diagnosed. The incidence of female breast and genital cancer is far lower in women with allergic and hyperthyroid conditions (group A) than in hypothyroid women or women with a partial thyroidectomy because of goiter (group B). Women belonging to group A have a much higher histamine content in their cells than women in group B, and the lipid content of the blood is much lower in group A than in group B. The more thyroid hormone circulates in the blood, the higher is the histamine content in the cells, the lower the level of the lipids, and the less tendency to cancer formation. The less thyroid hormone circulates in the blood, the lower is the histamine content in the cells, the higher the level of the lipids, and the greater the tendency to cancer formation. Intracellular protein-bound histamine is regarded as a defense hormone against cancer formation under the control of the thyroid hormone. Thyroid hormone, given in massive dosage in cases of inoperable cancer of the breast and genitals, slowed down cancer growth. Thyroid hormone in daily dosage ranging between 1 and 5 grains (65 and 320 mg.) has been given by Loeser since 1948 as a prophylactic against cancer recurrence after radical operations for breast or genital cancer and after deep x-ray treatment.

Isoniazid in Treatment of Genital Tuberculosis. A. Caballero. Riv. ital. ginec. **37:**138-157 (No. 2) 1954 (In Italian) [Bologna, Italy].

Isoniazid, alone or with streptomycin, was used to treat 40 women with tuberculosis of the endometrium in whom the diagnosis was established by biopsy. The cervix was also involved in 19 of the patients. A complete anatomic recovery—disappearance of the tubercle bacilli—was obtained in 90 days in the patients who received daily oral doses of 5 mg. of isoniazid per kilogram of body weight. Two patients who received twice as much isoniazid each day recovered in 70 and 75 days respectively. Those who were given 5 mg. of isoniazid per kilogram of body weight and 1 gm. of streptomycin every other day made a complete anatomic and functional recovery—endometrial function—in from 40 to 50 days. One patient who instead received 1 gm. of streptomycin every day recovered in 35 days. Patients in whom streptomycin, *p*-aminosalicylic acid, and amithiozone had earlier proved inadequate recovered in 45 days, suggesting that the bacilli were more sensitive to the action of isoniazid. Biopsy specimens were secured from the first four patients every 20 days and from the others every 30 days; the weight, blood findings, sedimentation rate, and urine were checked every 15 days. Fever dropped and disappeared within the first month of therapy except in two patients in whom it persisted in a mild degree for 2 and 2.5 months respectively. The sedimentation rate dropped gradually, becoming normal in most by the time the anatomic recovery was secured. Patients in whom the adnexa were involved had the highest initial values, and in these the sedimentation rate remained high, despite an initial drop suggesting that the inflammation was still present. There was a gain in weight ranging from 1 to 9 kg. (2.5 to 20 lb.) in 23 patients. No abnormalities were found in the urine. The general condition was improved in all. The author treated with isoniazid in daily doses of 5 mg. per kilogram of body weight four patients in whom laparotomy had disclosed peritoneal tuberculosis with involvement of the genital peritoneum. Fever disappeared within three weeks; the sedimentation rate became normal after 75 days; appetite was improved, and some gained as much as 9 kg.; and the abdominal disturbances diminished or disappeared. All the patients of this study tolerated the drug well and there were no side-effects. A follow-up of 15 of them one year later revealed no relapses when a biopsy was made of the endometrium and the cervix.

Pregnancy and Delivery with Double Malformation in Genital Tract. J. Østergaard. Ugeskr. læger **116:**1659-1667 (Nov. 25) 1954 (In Danish) [Copenhagen, Denmark].

Detailed report is given of seven patients with various forms of double malformation in the genital tract, verified by hysterosalpingography, observed during the last years in a place with about 600 deliveries annually. There were 12 pregnancies and 10 deliveries. Seven breech or transverse presentations were met with. Double malformation was diagnosed before delivery in only one instance. The anomaly, presumably hereditary, and important for sexual life, pregnancy, and delivery, is commoner than generally assumed and difficult to diagnose. Repeated deliveries with irregular position of the fetus in a patient or the patient's family should lead to examination with reference to possible double malformation.

PEDIATRICS

Endocardial Fibroelastosis. R. Lutembacher. Presse méd. **62:** 1824-1826 (Dec. 25) 1954 (In French) [Paris, France].

An opportunity for reviewing endocardial fibroelastosis was provided by the following case. A 6-month-old infant died suddenly in cardiac failure with cyanosis and dyspnea. The death was suspected of being unnatural, and accordingly a postmortem examination was performed, revealing fibroelastosis of the endocardium. This case is representative of the death from acute cardiac insufficiency caused by this disease in young children; the rapidity of the course of this disease is a function of the age of the patient, varying in inverse proportion. Auscultation may reveal nothing. Roentgenography shows considerable cardiomegaly. The myocardium is hypertrophied, especially in the left ventricle. The aspect of the endocardium is milky white, thickened, and smooth. The process is noninflammatory but shows proliferation of the collagen and elastic fibers. The myocardium is relatively free of involvement; its hypertrophy would seem to be a secondary phenomenon, and it is the fibroelastic condition of the endocardium that prevents proper functioning of the heart. However, in some cases, direct involvement of the myocardium could be incriminated. The disease cannot be of infectious origin; it is probably a malformation. The most convincing explanation of this is that the defect arises from a cardiac anomaly due to tissue heteropia.

Changing Status of Rheumatic Fever and Rheumatic Heart Disease in Children and Youth. H. M. Wallace and H. Rich. A. M. A. Am. J. Dis. Child. **89:**7-14 (Jan.) 1955 [Chicago].

Wallace and Rich analyze mortality data on rheumatic fever and rheumatic heart disease in New York City from 1940 through 1950. The data indicate that there has been a significant reduction in deaths due to rheumatic heart disease and rheumatic fever in children and youth in the past decade. During the same period, the diagnostic pattern of children seen in five cardiac consultation service clinics indicates a similar change,

with fewer children with rheumatic heart disease and more children without heart disease being seen. More children seen in these clinics are being recommended for educational placement in regular classes in the public schools, indicating either no cardiac handicap or a less severe one. The authors feel that several factors have contributed to this changing picture. The general level of child health has greatly improved. Improvement in social conditions, in the standard of living, and in nutrition and some elimination of slum areas are all possible factors. Many infections, including those due to streptococci, are now treated earlier and more effectively by the sulfonamide drugs and antibiotics. Programs of public health organizations should put emphasis on early case finding, the securing of accurate diagnosis in all children suspected of having rheumatic fever or heart disease, high quality hospital and convalescent care, good follow-up, appropriate educational placement, consideration of vocational aspects, and the encouragement of the wider use of prophylactic agents, in an effort to prevent recurrences of rheumatic fever.

Evaluation of the Flush Technique for the Determination of Blood Pressure in Infancy. M. P. Sullivan and M. Kobayashi. Pediatrics **15:**84-87 (Jan.) 1955 [Springfield, Ill.].

By means of the flush technique, three systolic blood pressure readings were taken in the right arm and leg of 160 Japanese infants of approximately 9 months of age. Analysis of the data obtained on 103 babies who were quiet or nursing when all determinations were made showed the following results: 1. A sex difference in systolic blood pressure could not be demonstrated by statistical methods; there was no apparent relationship between blood pressure and height or weight. 2. No difference could be demonstrated between arm and leg pressures by statistical methods. 3. The difference in systolic pressures among infants in this study was highly significant. This variability among patients was greater than the variability among the three observations on an extremity of an individual patient. 4. The method may be considered a satisfactory clinic or office procedure if its limitations are recognized. One blood pressure reading on a patient by this method is of little value. A minimum of three readings should be obtained and averaged. Five readings are recommended for routine blood pressure determinations. For more exacting studies, eight readings might be taken and averaged.

Effect of Adrenocorticotropic Hormone (ACTH) and Cortisone on Proteinuria and Hematuria in the Nephrotic Syndrome. W. Heymann, C. Gilkey and M. Salehar. Pediatrics **15:**49-53 (Jan.) 1955 [Springfield, Ill.].

Fifteen children with the nephrotic syndrome were treated with 22 courses of either corticotropin or cortisone. Three children failed to have a diuresis during four courses of treatment. No decrease in proteinuria was noted. Eighteen courses of hormone treatment resulted in diuresis in 12 patients. A decrease in proteinuria preceded diuresis in each instance. A relationship between severity of hypoproteinemia and onset of diuresis, once proteinuria has started to decrease, was established. It is concluded that one of the important actions of corticotropin or cortisone in inducing diuresis is concerned with the decrease in proteinuria, resulting in increasing plasma protein concentration and oncotic pressure. The effect of these hormones on hematuria in nephrosis has been noted during four courses of treatment. In these proteinuria decreased appreciably. In four instances hematuria persisted and proteinuria decreased only slightly or not at all.

Risk of Developing Tuberculosis Among Children of Tuberculous Parents. L. D. Zeidberg, A. Dillon and R. S. Gass. Am. Rev. Tuberc. **70:**1009-1019 (Dec.) 1954 [New York].

The data presented were collected in Williamson County, Tennessee, for a period of 22 years. Some of the information was derived from the direct observation of the children of tuberculous parents; the remainder is based on historical information obtained at the time that the tuberculous household first came to the attention of the investigators. The analyses are concerned chiefly with the experience of 733 children of white tuberculous parents who had acid-fast organisms in their sputum and who were also the "index cases" of their households. The tuberculosis attack rate was 3.3 per 1,000 person-years among children of tuberculous parents with sputum positive for acid-fast bacilli, compared with a rate of 1.8 for children of a tuberculous parent in whom no bacilli were demonstrated. In the former group the highest rates were observed in those less than 5 years old and in those 15 to 24 years of age. In the latter group, attack rates were extremely low in persons less than 15 years of age but then rose and reached a peak at 25 to 34 years. The risk of developing tuberculosis after removal from the household, although not as great as during residence in the household, was nevertheless of significant proportions. During household exposure to a parent with "open" tuberculosis, the disease was more apt to develop in males less than 5 years of age while females were at greatest risk in the 15 to 24 year period. Children exposed during infancy to a tuberculous parent with sputum positive for acid-fast bacilli had a short incubation period. Those exposed for the first time between the ages of one and 14 years did not manifest disease until after 15 years of age. Among those exposed for the first time at the age of 15 or later, the incubation period was again short, with new cases developing rapidly. The authors feel that children of parents with "open" tuberculosis should be observed closely. In infancy boys require closer observation; during adolescence and early adulthood, however, girls appear more vulnerable to attack. Periodic examination of children should not cease after they have broken contact with the tuberculous parent by moving out of the household.

Plasma 17-Ketosteroids of Full-Term and Premature Infants. L. I. Gardner and R. L. Walton. J. Clin. Invest. **33:**1642-1645 (Dec.) 1954 [New York].

The adrenal cortex of the newborn infant shows a relative lack of responsiveness to the administration of adrenocorticotropic hormone. This, together with the presence of the fetal reticular zone of the adrenal cortex and the recent report of low concentrations of hydrocortisone-like substances in the plasma of newborn infants are all reminiscent of the findings in infants and children with congenital adrenal hyperplasia. Since children with congenital adrenal hyperplasia have been shown to have markedly elevated concentrations of plasma neutral 17-ketosteroids, it was thought desirable to investigate the concentrations of these steroids in the plasma of newborn infants. Gardner and Walton analyzed for neutral 17-ketosteroids plasma samples from 19 full-term, newborn infants, and from 20 premature infants. The premature infants had attained weights ranging from 793 to 2,381 gm. when the samples were taken. The full-term newborn infants showed plasma 17-ketosteroid concentrations in the first 48 hours of life that were in excess of the mean value for nonpregnant women. These plasma concentrations then rapidly fell to unmeasurable values by the end of the first week of life. The premature infants showed maximal values higher than the values shown by the full-term infants, and measurable concentrations were still found up to 42 days of age. There appears to be as yet no adequate explanation for the differences found between the full-term and premature infants.

Palpebral Gangrene in Newborn Infants. R. P. Pereira and A. Conti. Arch. oftal. Buenos Aires. **29:**503-510 (Sept.) 1954 (In Spanish) [Buenos Aires, Argentina].

Gangrene of the eyelids is an extremely rare condition in newborn infants. In the few cases reported in the literature, the condition was caused by diphtheria, purulent ophthalmia, or gangrenous dermatitis of syphilitic origin. In all cases the disease followed a rapid course to a fatal end. The subject of this report was an infant 2 weeks old, who was born slightly premature and dystrophic. The parents had no syphilis. The mother had arterial hypertension and diabetes. She had four normal children before her pregnancy with the patient. The patient did not gain weight after birth and cachexia developed. A little red spot appeared on the 10th day after birth on the lower eyelid of the left eye. It rapidly diffused, manifesting signs of gangrene, and closed the eye. Penicillin by parenteral route and polyvitamins were without effect. The patient died one week after hospitalization and 12 days after appearance of the lesion. Palpebral gangrene of the eyelids is a grave lesion. Inanition caused by the disease and

leukopenia are the main causal factors. The prognosis has slightly improved since the discovery of antibiotics. The treatment consists of local and general administration of penicillin and sulfonamides. Early administration of antibiotics may restrict further progress of gangrene, causing rapid elimination of the necrotic tissue, with consequent improvement in the general condition of the patient. At this stage of the treatment, there are still two possibilities: Either dystrophy improves and the life of the patient is spared or it does not and the patient dies because of the inanition caused by the disease. Surgical intervention for palpebral gangrene is indicated in children and in young adults after failure of chemical therapy and antibiotic therapy, provided the acute course of the disease depends on deep changes in the general condition of the patient rather than on the virulence of the local disease. The operation is done with the patient under a general anesthesia. It consists of removal of all necrotic tissue down to normal tissue and of dusting of the surgical area with penicillin or sulfathiazol or else lavages with solutions of antiseptic substances. After the operation, stimulants and vitamins are given. The operation calls for further plastic surgery for reconstruction of the eyelids.

DERMATOLOGY

Melanotic Freckle (Hutchinson), Mélanose Circonscrite Précancéreuse (Dubreuilh). J. V. Klauder and H. Beerman. A. M. A. Arch. Dermat. **71:**2-10 (Jan.) 1955 [Chicago].

The occurrence of malignant melanoma arising from the pigmented lesion that Hutchinson first described as senile freckle or infective melanotic freckle and which was later termed by Dubreuilh mélanose circonscrite précancéreuse is reported in three women between the ages of 60 and 76 and one 55-year-old man. In the three women the lesion appeared on the upper region of the right side of the face, on the ear, and on the eye respectively. In the man, the lesion appeared on the midportion of the outer aspect of the leg. The duration of the lesion varied from 10 to 25 years in the three women and was 3 years in the man. The entire lesion was destroyed by electrodesiccation, and the operative area was given a single total air dose of 1,000 r in the two women with the lesions on the face and the ear. In the woman with the eye lesion, involving the bulbar conjunctiva, caruncle, semilunar fold, and both the upper and lower lids, the eye was enucleated. The lesion in the man was excised with a wide margin of normal skin. After this excision, a total air dose of 2,000 r was given in multiples of 200 r, three times a week. Nine years after the excision of the lesion, the patient died of an acute heart attack; he led an active life up to the time of his death, there was no local recurrence, no regional lymph node enlargement, or other evidence of metastasis. A fifth case of melanotic freckle on the left cheek of a 75-year-old woman is reported; this case is unique because of the presence of a small verrucous lesion on the surface of the melanotic freckle. Biopsy of the lesion did not show any evidence of malignant melanoma. Microscopic examination of the entire lesion in the four cases of malignant melanoma arising from the melanotic freckle showed that, in contrast to the usual picture of junction type nevus, the nonactive melanotic freckle may have little or none of the phenomenon of segregation. It is important, therefore, from the standpoint of prognosis, that not only the tumor mass but also the nonelevated pigmented part of the lesion should be studied microscopically. The location of the lesion (the face), the age of the patient (if beyond middle age), the history, and the clinical appearance of the original pigmented lesion are important considerations in differential diagnosis. The melanotic freckle is presented in two stages, the pigmented precancerous stage and the tumor stage or malignant melanoma. The authors see no objection to destroying by electrodesiccation or by surgical excision the primary pigmented patch in absence of tumor formation; subsequently, newly appearing areas of pigmentation could likewise be destroyed. If the patient is aged and the lesion is on the face, the authors would not insist that the pigmented patch in the nontumor stage be destroyed. Apparently there is no necessity of subjecting patients with facial lesions of the disease to radical surgical procedures or extensive lymph node dissection. If the melanotic freckle is on an extremity, in consideration of the shorter period of the precancerous stage and greater likelihood of metastasis in the tumor stage, it would appear desirable routinely to excise or destroy by electrodesiccation the pigmented lesion. If the tumor stage has ensued, excision of the entire lesion followed by roentgen therapy may suffice. If the lymph nodes are involved, the same procedure with lymph node dissection is indicated.

Studies on the Prophylactic Effect of Locally Applied Antibiotics in Experimental Syphilis. O. R. Aavik. J. Invest. Dermat. **23:** 497-501 (Dec.) 1954 [Baltimore].

At the meeting of the Subcommittee on Venereal Diseases, National Research Council, held in Washington, D. C., in May, 1952, it was the consensus that it would be advisable to test the potential value of the newer topical antibiotic preparations for their effect in preventing syphilitic infection. There was agreement that such a study could be carried out on rabbits. In the first experiments the penis of healthy adult rabbits was exposed and the edge of the foreskin was crushed with a hemostat. This trauma caused a local hematoma. Later it was found that mildly stroking the inner edge of the foreskin three times with a gauze pad that was moistened with sodium chloride solution constituted sufficient trauma to yield 100% typical chancres after the surface of this area was suitably infected. Treponemal suspensions were prepared and made to contain an average of five organisms per darkfield initially. Cotton pledgets were soaked in this treponemal suspension, inserted into the preputial sac, and left in site for three hours. At first 9 to 10 animals were infected for each experiment. Three animals were treated with white Vaseline, three or four with the test substance, and three were not treated at all. The ointments in the quantity of about 1 gm. were spread all over the exposed area. Later, when it became evident that Vaseline did not exert any prophylactic effect, the blank controls were eliminated. After application of the ointments the animals were inspected every two to three days. The incubation period for development of a clinically visible lesion was found to range from 24 to 63 days. Darkfield preparations were made from all suspicious lesions. Ointments containing Terramycin, Aureomycin, erythromycin, penicillin, neomycin, bacitracin, and hexachlorophene soap were tested. None of the antibiotic ointments, except penicillin, had a satisfactory prophylactic effect. It should be emphasized, however, that the test conditions have been rather severe. However, for an orientation study it seemed to be more appropriate to use such severe conditions. With this method the control groups yielded clinically typical chancres in 96% of the cases. The apparently satisfactory results with penicillin ointment require comment. The absence of a clinically visible lesion does not exclude the possible occurrence of a silent infection. This possibility was not pursued further.

The Effect of X-Rays on Experimentally Produced Acute Contact Dermatitis. T. S. Kemp and A. M. Kligman. J. Invest. Dermat. **23:**423-425 (Dec.) 1954 [Baltimore].

Kemp and Kligman describe experiments that they undertook to ascertain whether conventional superficial x-rays are therapeutically effective in contact dermatitis of the allergic type. They found that superficial x-rays of the conventional and low voltage type, given according to different dosage schedules and in different amounts, did not alter significantly the course of acute eczematous contact dermatitis of the allergic type produced in subjects experimentally sensitized to 2:4 dinitrochlorobenzene. These findings raise a serious doubt of the worth of x-rays in the therapy of acute allergic contact dermatitis.

Investigations on pH Value of the Skin Under Plaster-of-Paris Casts. C. G. Schirren, F. Schedel and H. Kolbeck. Klin. Wchnschr. **32:**1086-1087 (Dec. 1) 1954 (In German) [Berlin, Germany].

The pH values established by Schirren and associates are average results of 840 individual determinations that they made on 70 plaster casts on the leg, dorsum of foot, thigh, upper arm, and lower arm, inclusive of the corresponding control sites on the side of the body not covered by a plaster cast. The average pH value under plaster casts of the leg over the tibia was pH 5.01, whereas the corresponding value on the healthy side was

pH 5.10. On the dorsum of the foot the values were pH 4.93 and 4.98; on the thigh pH 4.84 under plaster and pH 5.01 on the side not in a cast; on the lower arm pH 5.18 and 5.10, and on the upper arm pH 5.24 and 5.21. These values show that the pH values remained rather constant and unchanged. The authors conclude that the inhibition of cutaneous perspiration is not so great that shifts in the pH values result as is the case in the presence of physiological gaps in the acidity cover, for instance in the axillas. Furthermore, the surface pH values of the skin are largely independent of the blood perfusion of the skin or of the subcutaneous soft tissues. No conclusive answer is possible to the question whether the constancy of the cutaneous pH values explains the rarity of pyodermas under plastic casts.

Benign and Malignant Nevus Cell Tumors. L. Nitter. Tidsskr. norske lægefor. **74:**740-742 (Dec. 1) 1954 (In Norwegian) [Oslo, Norway].

Almost everybody has one or more brown, often slightly elevated pigment collections in the skin. In general they are benign; occasionally they may develop into malignant tumors. In Norway only about 70 new cases of the nevus cell tumor form are reported annually. The so-called prepubertal melanomas are an important type of pigmented nevi; in spite of a positive histological picture they do not act like malignant tumors. In connection with puberty a change may set in and malignant nevus cell tumors may develop immediately after puberty from common pigmented nevi. In their development they are thought to be subject to hormonal regulation. If malignant melanomas develop from nevi during pregnancy they grow more unchecked than at any other time in life. Malignant melanomas also develop in many women at the climacterium. Hormone therapy has been without effect. All dark pigmented suspect nevi should be removed in childhood (Pack). Up to 50% of the patients with malignant nevus tumors can recall some injury to the preexisting nevus, as chronic irritation from clothing, infections, and traumas of other kinds. More than 50% of the malignant melanomas develop from nevi present since birth or shortly thereafter; a smaller number develop from nevi originated later in life. The relatively few so-called unpigmented nevi present great difficulties. In the main the author's advice is: Leave the common brown pigmented nevi alone, but when some change suddenly appears, as growth, darkening of color, bleeding, itching, and other irritations, the nevi should be removed wherever they are located. All elevated nevi should be removed which because of their situation are constantly exposed to irritation. All nevi removed in prophylaxis should be examined microscopically. If microscopic examination of a nevus is desired the entire tumor must be excised. If it is clinically suspect, immediate radical removal of the entire primary tumor is indicated. Malignant nevus tumors constitute about 10% of all primary tumors in the skin and, according to the Norwegian Cancer Register, represent about 1.2% of all reported cases of cancer. The importance of immediate treatment is emphasized. Although these tumors should be among the most accessible forms of cancer for radical primary excision, they belong to the tumor groups with the lowest rate of recovery. In the Norwegian Radium Hospital prophylactic lymph node irradiation as well as postoperative irradiation corresponding to the seat of the primary tumor and the lymph node region have in part given encouraging results. The surgical intervention should not be so great that radiotherapy cannot be continued postoperatively immediately after the primary intervention. On change into malignant growth a nevus first grows locally, then invades the surrounding skin and subcutaneous tissue. In about 25% of the cases it is primarily transplanted by the blood stream to liver, lungs, heart, and so on; there is no known therapy for this type. In over half the cases, however, the path is to the nearest lymph nodes; here treatment must be started at once. Finally, there is a small group that gradually recurs with upward spread, without special speed, until after four or five years the whole explodes with general metastases. From 1932 to 1953, 393 patients with malignant nevus tumors were treated in the Norwegian Radium Hospital. Since 1948, about 40 new patients have been admitted annually. Of the 192 treated before 1948, 24% were living in January, 1954. Since early diagnosis and primary treatment are so important, it is in the first instance the practitioner, who is the first to see the patient, who can contribute to lowering the death statistics in this insidious cancer form.

Diffuse Melanosis in Melanosarcoma. I. S. Møller. Nord. med. **52:**1620-1621 (Nov. 18) 1954 (In Norwegian) [Stockholm, Sweden].

Secondary affection of the skin in melanosarcoma usually appears in the form of more or less multiple skin metastases. The case here described of diffuse melanosis with melanoderma after melanosarcoma is the 12th such case to be published. Dyspeptic symptoms set in four years after the removal of a melanosarcoma, and the patient's skin became darker. The condition worsened, and pigmentation increased. The tentative diagnosis of hematochromatosis was rejected. Skin biopsy revealed diffuse melanoderma. At autopsy metastases to liver, spleen, lymph nodes, and peritoneum were found, also minimal metastases in the subendocardial connective tissue, adrenals, bone marrow, and pleura, but none in the skin.

Mechanism of Endocrine Control of Melanin Pigmentation. A. B. Lerner, K. Shizume and I. Bunding. J. Clin. Endocrinol. **14:**1463-1490 (Dec.) 1954 [Springfield, Ill.].

The melanocyte-stimulating hormone (MSH) from the pituitary gland causes darkening of human skin and nevi and formation of new nevi. The authors administered this hormone to nine subjects. Three had vitiligo, which became more noticeable after administration of the hormone, because the depigmented skin did not darken, while the normal skin did; one patient noted slight repigmentation around the hair follicles of the vitiliginous skin. A patient with pallor due to hypopituitarism experienced hyperpigmentation until he resembled a patient with adrenal cortical hypofunction (Addison's disease); such effects disappear after the administration of the hormone is discontinued. Massive doses of the hormone were given to one subject, and increased pigmentation was observed within a few hours. When the melanocyte-stimulating hormone was given intramuscularly, from 1 to 4% was excreted in the urine. After intravenous administration, about twice as much was excreted. The action of other hormones is related to that of the melanocyte-stimulating hormone. Hydrocortisone and cortisone probably inhibit the release of this hormone from the pituitary gland. Arterenol and epinephrine can block the local action of the hormone on melanocytes, the pigment cells. The first factor is of clinical significance, because cortisone and hydrocortisone can prevent the development of hyperpigmentation in patients who have undergone bilateral adrenalectomy and in patients who have adrenal cortical hypofunction and can decrease pigment already present in this disease. The action of epinephrine and arterenol, although these substances are potent in vitro, has not yet proved to be of clinical significance. In addition, progesterone, which causes darkening of frog melanocytes, may have an effect on human melanocytes. The melanocyte-stimulating hormone seems to be a distinct pituitary hormone. Pigmentation associated with the clinical administration of corticotropin (ACTH) is probably due to melanocyte-stimulating hormone contamination. Because of the possible relationship between this hormone and malignant melanomas, and the role of this hormone in a variety of pigmentary disorders, it is important to determine the chemical structure of the melanocyte-stimulating hormone. Such knowledge might provide insight into its mechanism of action.

Determination of Melanocyte-Stimulating Hormone in Urine and Blood. K. Shizume and A. B. Lerner. J. Clin. Endocrinol. **14:**1491-1510 (Dec.) 1954 [Springfield, Ill.].

Quantitative assay procedures for determining the melanocyte-stimulating hormone (MSH) in the urine and blood, with isolated frog skin, are described. An increase in blood concentration of the hormone is associated with an increase in its urinary excretion. The tests appear to be specific for the melanocyte-stimulating hormone. Epinephrine, arterenol, hydroxytyramine, serotonin, ergotamine derivatives, and Mesantoin (5-ethyl-3-methyl-5-phenyl-hydantoin), which ordinarily affect frog melanocytes, do not interfere with the assays because they are not

extracted with the melanocyte-stimulating hormone. The concentration of the hormone in urine and blood is the same for normal males and females. The 24-hour urinary excretion values range from 7.5 to 47.5 units, with an average of 27.7 units. In blood the range of the hormone is from 0.4 to 2.2 units per milliliter, with an average value of 1.3 units per milliliter. During pregnancy, excretion of the hormone becomes elevated at the end of the second month and continues to increase until term. After delivery there is a rapid return to normal within a few days. Seven of 12 patients with adrenal cortical hypofunction (Addison's disease) and 4 out of 8 who had had bilateral adrenalectomies excreted increased quantities of the melanocyte-stimulating hormone. Some of these patients may have excreted normal amounts of the hormone because they were receiving cortisone. The level of the hormone was elevated also in single patients with each of the following conditions: new lentigines, alopecia areata totalis, and retinitis pigmentosa. Negroes, albinos, and patients with vitiligo showed normal excretion values of the hormone. Two of 8 patients with decreased pituitary function excreted decreased amounts of the melanocyte-stimulating hormone. Administration of cortisone to a patient with high levels of the melanocyte-stimulating hormone in the blood and urine reduced the hormone concentration to normal. After adrenalectomy the blood level of the hormone increased markedly in a dog and returned to normal when cortisone was administered.

OTOLARYNGOLOGY

Effectiveness of Penicillin in Prophylaxis and Treatment of Severe Acute Otitis Media, Mastoiditis, and Their Intracranial Complications. E. Lüscher and G. Gentinetta. Schweiz. med. Wchnschr. **84:**1331-1335 (Nov. 27) 1954 (In German) [Basel, Switzerland].

Of 602 patients with acute otitis media who were admitted to the otolaryngological clinic of the University of Basel, Switzerland, between 1937 and 1940, i. e., before sulfonamide therapy was practiced, 230 (38.5%) were operated on and 62 (10.5%) had intracranial complications, such as epidural abscess, leptomeningitis, sinus thrombosis. Death resulted from otitis media or its complications in 17 (2.8%). Of 505 patients with acute otitis media who were admitted to the same clinic between 1941 and 1944, i. e., the period during which sulfonamide therapy was practiced exclusively, 123 (26.3%) were operated on, 21 (4.2%) had intracranial complications, and death resulted from otitis media or its complications in 4 (0.8%). Of 189 patients with acute otitis media who were admitted to this clinic between 1949 and 1952, i. e., the period during which penicillin therapy was practiced, 47 (24.9%) were operated on, 11 (5.7%) had intracranial complications, and not a single death resulted from otitis media or its complications. The statistical data of these three four-year periods of different treatment of acute otitis media show that the early treatment of acute otitis media with an adequate dose of penicillin (i. e., from the beginning 1 million units for adults and a correspondingly smaller dose for children) and for a sufficient length of time (in accordance with the clinical course and definitely for a longer period than two to three days) has proved to be extremely effective. The acute otitis media has a much milder course, so that fewer patients require hospitalization. Of 47 patients with mastoiditis who were admitted to the clinic between 1949 and 1952, 29 had to be operated on because of softening of bone or intracranial complications, and none of these 29 patients had been treated with sulfonamide compounds or penicillin. In 16 of the remaining 18 patients, sulfonamide or penicillin therapy had been instituted too late or with insufficient dosage, and only 2 patients were resistant to penicillin. The mortality rate of acute otitis media was reduced to practically zero. Consequently, treatment with penicillin or with other antibiotics should be instituted as soon as possible in every case of severe otitis media, while in the later course of the disease, particularly when mastoiditis threatens, penicillin therapy may be practiced only when strict clinical control is provided for. Treatment with penicillin certainly is not a substitute for mastoidectomy in mastoiditis. Penicillin is mostly superior to sulfonamide therapy, although in many cases the latter may be of equal value. Other antibiotics are indicated in those cases in which penicillin fails. Only the future will show whether the untoward reactions to penicillin, particularly allergization, as well as the occasional increase in resistance of the pathogenic agents, should require the systematic application of other antibiotics or an increased use of sulfonamide compounds.

Acoustic Neuroma: Early Diagnosis. F. A. Elliott and W. McKissock. Lancet **2:**1189-1192 (Dec. 11) 1954 [London, England].

The postoperative mortality and morbidity in patients with acoustic neuromata are disappointingly high, especially in view of the benign character and accessibility of most of these tumors. On the basis of three case histories, Elliott and McKissock show that it is possible to make a presumptive diagnosis of acoustic neuroma at a stage when the clinical features are almost entirely confined to disturbances of hearing and labyrinthine function and that in such circumstances the tumor can be removed, without increasing the preoperative level of deafness and without damaging the facial nerve or neighboring structures. The authors describe the histories of the three cases in which diagnosis was made at a stage when only the seventh and eighth nerves were involved by the growth. The tumors were removed without increasing the preoperative level of deafness and without causing facial paralysis. There is evidence that about 75% of patients with acoustic neuroma have, as their first symptoms, either deafness or tinnitus or vertigo, or a sense of disequilibrium short of vertigo. Usually the patient first seeks advice from an otologist, and unless the tumor has grown large enough to cause significant symptoms and signs, the clinical picture at this stage may not greatly differ from that seen in the commoner diseases of the cochlea. A complete neurological examination, including caloric and audiometric testing, of all patients with perception deafness is hardly possible; but a careful history, and an examination restricted to gait, stance, and the fifth, seventh, and eighth cranial nerves, will usually suffice to pick out the patients who require complete otological investigation. The authors stress particularly the diagnostic value of the loudness balance test. In cochlear disease the impairment of hearing present at threshold diminishes as the intensity of the stimulus is increased, until a point is reached when the sound is heard equally well by both ears, or may even appear louder on the affected side. This phenomenon, known as recruitment (and overrecruitment) does not occur in eighth-nerve lesions, although in acoustic neuromas partial recruitment may occur. The presence of full recruitment in a case of perceptive deafness argues against the presence of an acoustic neuroma. The authors discuss the impairment of the corneal reflex in two of their patients. Depression of the corneal reflex in early cases is due to interference with the motor part of the reflex arc in the facial nerve and does not necessarily imply damage to the trigeminal sensory root. Damage to the vestibular component of the eighth nerve can cause unsteadiness of stance and gait, and these symptoms do not necessarily indicate interference with the cerebellum, though they may complicate the cerebellar ataxia seen in more advanced cases.

THERAPEUTICS

Diuretic Action of Rauwolfia Serpentina. S. Drovanti, C. Cei and C. Strada. Minerva med. **45:**1403-1407 (Nov. 28) 1954 (In Italian) [Turin, Italy].

The effect of Rauwolfia serpentina on the renal function was studied in dogs that were given intravenously a total dose of from 4 to 20 mg. of total alkaloids of the drug in distilled water. Diuresis increased in all the animals, and this increase is ascribed partly to hyperfunction of the glomeruli and partly to hypofunction of the tubuli. There was, in fact, in the animals a 40% increase of the glomerular filtration and a 2.13% reduction of the tubular reabsorption. The authors attribute this to a decreased tone of the afferent arteriole, while that of the efferent arteriole was unchanged. In addition to this particular tone of the afferent arteriole, there were also special new conditions of the water-sodium chloride balance. The plasma and blood flow to the kidneys was increased by 8 and 10% respectively. The blood sodium levels tended to decrease, whereas those of potassium tended to increase. This inverse ratio of sodium to potassium was correlated more with the increase of the latter than

with the decrease of the former. The increased blood potassium values were due not to a retention of the electrolyte—its excretion in the urine was increased—but rather to its passage from the intracellular to the extracellular area. The picture of renal excretion of the electrolytes was comparable to that seen in cases of increased vagotonia and arterial hypotonia. The nitrogen content of the blood was decreased whereas its urinary excretion was increased. This was the result of the increased filtration. The quantity of nitrogen eliminated through the urine was directly proportional to the quantity of urine: its urinary concentration did not undergo particular increases because of the homogeneous diffusibility of the substance in the organic fluids. According to the authors, the particular behavior of the arterioles suggests that the renal function had adapted itself to the new state of water balance and that it had done this by eliminating the excess of water or salts so as to bring about a new state of homeostasis in connection with the new conditions induced by the introduction of total alkaloids of Rauwolfia serpentina.

Physiopathology and Treatment of Acute Barbiturate Poisoning. C. Campana. Policlinico (sez. prat.) **61:**1317-1327 (Oct. 4) 1954 (In Italian) [Rome, Italy].

Coma that follows the ingestion of excessive amounts of barbiturates is characterized by depression of the respiratory center, with a resultant anoxia caused mainly by the slow elimination of the drug through the kidney. Treatment, which should be instituted as soon as possible, should therefore aim at eliminating the drug, influencing the symptoms, and administering antagonistic medicaments. To hasten the elimination of the barbiturate, some authors use immediate gastric lavage. However, when the patient is already unconscious, the procedure is not only useless but it is harmful, because it facilitates the onset of pulmonary complications. Gastrointestinal peristalsis is better restored by intramuscular injections of 0.5 mg. of neostigmine every four hours. Some authors perform spinal puncture and drainage and introduce isotonic sodium chloride solution at 37 C. However, this too is considered useless except perhaps for cases in which cerebral edema is present. Withdrawal of blood is dangerous, because it aggravates the hypotension and the anoxia. The most effective means is the administration by slow phleboclysis of large amounts of a 5% glucose isotonic sodium chloride solution. Recently Kyle and his associates accelerated the removal of the barbiturate by means of an artificial kidney, which proved of great value. In Italy, however, the artificial kidney is available only to few centers. The symptomatic treatment, which in many instances is sufficient by itself to save the patient, aims at the respiratory disturbances. To insure adequate airway the mucus is removed from the larynx, the trachea, or the lungs, in this case with bronchoscopy if necessary. If needed, intratracheal intubation is resorted to. Oxygen mixed with carbon dioxide should be given continuously until consciousness is regained, cyanosis disappears, and respiration is restored to normal. Penicillin and dihydrostreptomycin should be given early. To prevent hypostatic congestion and atelectasis, the patient's position should be changed every hour and his body temperature should be watched carefully. When severe peripheral collapse is present, plasma or blood transfusions are performed, and an arterenol solution is also given by slow phleboclysis or subcutaneous injections. To neutralize the increased capillary permeability, vitamin C and rutin are administered. The specific treatment consists in administering such antagonistic drugs as strychnine, picrotoxin, amphetamine, metrazole, and others. With regard to this treatment there are today four trends. One advocates the use of strychnine, a second that of picrotoxin and/or metrazole, another that of amphetamine, and the fourth, originated by Nilsson, opposes the use of all central analeptic agents. Nilsson asserts that even in the severest cases symptomatic treatment alone is sufficient.

First Clinical Experience with Intravenous Use of Chloramphenicol Succinate. R. Di Guglielmo and G. Cangi. Minerva med. **45:**1398-1403 (Nov. 28) 1954 (In Italian) [Turin, Italy].

The effects of chloramphenicol succinate given rapidly by two daily injections (in a 10% solution of isotonic sodium chloride solution) or slowly by phleboclysis (in 250 cc. of glucose solution) were studied in 18 patients, consecutively admitted, at the University of Florence. The initial doses were small in order to determine the minimal effective dose for this route of administration. Although the results were equally good with both methods, it might be better to give the drug by injection, because the patients accept this more willingly and also because the possible febrile reactions of the second method, owing to the presence in it of pyrogenic substances, are prevented. The authors suggest an initial dose of two 100 mg. injections on the first day, increasing it gradually 200 mg. each day until the optimal dose is reached. The results were particularly good in patients with nonparasitic acute or chronic enterocolitis. Fever disappeared on the second day of therapy and the general condition began to improve in one patient with Q fever in whom penicillin and streptomycin had been ineffective. There was a good improvement in one patient with chronic cholecystopathy and dyspepsia, and one patient with an aortic defect and infection caused by Streptococcus viridans was also greatly benefited. The condition of three patients with fever of diverse origin (pulmonary neoplasm, suppuration in Hodgkin's disease, and rheumatic endocarditis) was unchanged. The therapy was always well tolerated, and there were no local or general side-effects. Because smaller doses of chloramphenicol succinate are required when it is given intravenously, the danger of side-effects is smaller and the therapy is more economical. Further clinical trial is needed.

Combined Chemotherapy of Pneumonia in Children of Various Ages with a New Domestic Antibiotic, Biomycin. G. N. Speransky, R. L. Hamburg and E. I. Pavlova. Pediatriya **3:**11-17 (March-April) 1954 (In Russian) [Moscow, Russia].

A new Soviet-made antibiotic, biomycin, was used in the treatment of 80 infants with pneumonia. All but 11 of these patients were less than one year old. About half of them were poorly nourished. Combined therapy with penicillin and biomycin proved to be the treatment of choice. It exercised a marked influence on the majority of the patients, even in cases of extremely severe illness, such as pneumonia of virobacterial origin superimposed on a background of viral influenza, and severe forms of pneumonia in weak children, accompanied by toxic dyspepsia or dysentery. Biomycin was also effective in penicillin-resistant forms of pneumonia. Satisfactory results were obtained in 62 children. There was one death. With biomycin therapy, improvement in the general condition and the reduction of toxic symptoms progresses faster than temperature reduction. A dose of 50 units per kilogram of body weight every 24 hours is excellent. Side-effects are rarely seen. The fact that biomycin can be orally administered makes it possible to avoid hurting seriously ill children. Two illustrative cases are presented.

Choleriform Syndrome as Complication of Antibiotic Therapy. H. Helmig. Schweiz. med. Wchnschr. **84:**1382-1385 (Dec. 11) 1954 (In German) [Basel, Switzerland].

Of 58 patients who were subjected to intra-abdominal operations at the surgical clinic of the canton hospital in Münsterlingen, Switzerland, and who were given oxytetracycline (Terramycin) for preoperative sterilization of the gastrointestinal tract or because of preoperative or postoperative infection with Escherichia coli, 28 had undesirable side-effects of the antibiotic therapy consisting of diarrhea of varying intensity and duration. The daily dose of the antibiotic varied from 250 mg. to 3 gm., but most of the patients received 1 gm. daily, with a total dose of 6.5 gm. and an average six day duration of the treatment. Eleven of the 28 patients had mild diarrhea, with soft to liquid stools but without discoloration; 14 had severe diarrhea; and 3, who had severe diarrhea with stools containing mucus, pus, and larger or smaller amounts of membranes, died. The three fatal cases occurred in patients between the ages of 67 and 74 who were operated on for carcinoma of the stomach, carcinoma of the rectum, and perforated diverticulum of the sigmoid, respectively, and who were given 500 mg. of oxytetracycline twice daily by drip infusion. Bacteriological analysis of the feces was performed in one of the three patients only and revealed the presence of hemolytic micrococci (staphylococci) in addition to E. coli mucosum. Autopsy showed severe ulcerative colitis in two patients and diffuse necrotic pseudomembranous colitis in one;

a superinfection with micrococci seemed, therefore, likely in all three cases. The term "choleriform syndrome" was coined by the French worker Janbon for this type of micrococcic enterotoxic reaction, which also was observed by the Americans Dearing and Heilman. Two additional patients are reported on who underwent ileostomy and appendectomy, respectively, and were given postoperatively two short courses of 3 and 2 gm. of oxytetracycline on the 3rd to the 5th, and on the 9th and 10th postoperative day respectively. Both patients did not have any untoward reactions to the antibiotic therapy. The administration of the antibiotic for a maximum of three days, and again after a sufficient interval, i. e., after the recurrence of the normal intestinal bacterial flora, corresponds to the present-day knowledge of the disappearance of the normal and the occurrence of abnormal bacterial colonies in the intestine under the influence of antibiotics. The author agrees with the American workers that should untoward reactions to the antibiotic therapy occur, despite the described mode of administration, they will subside within a short time after the oral administration of 300 to 400 mg. of erythromycin four times daily as soon as the first undesirable symptoms occur. Preoperative administration of slightly soluble sulfonamide compounds also is recommended for the prevention of the choleriform syndrome.

PATHOLOGY

Positive Direct Coombs Test Induced by Phenylhydrazine. E. E. Muirhead, M. Groves and S. Bryan. J. Clin. Invest. **33**:1700-1711 (Dec.) 1954 [New York].

The Coombs or antiglobulin test was introduced for the detection of antibodies to erythrocytes of a type termed "incomplete antibodies." The indirect Coombs test has gained wide application in the detection of the antibodies to various erythrocytic antigens and in the cross matching of blood for transfusions. The direct Coombs test has become a diagnostic and investigative tool in hemolytic disease of newborn infants after incompatible blood transfusions and in the acquired hemolytic anemias, idiopathic or secondary types. All of these conditions in man, when associated with positive direct and indirect Coombs' tests, have been interpreted to be the result of immune mechanisms, either of the isoimmune or autoimmune type. The authors describe observations on dogs that had been given intravenous injections of a 1 to 2% solution of phenylhydrazine hydrochloride. A positive direct Coombs test was produced in the dog by means of this drug. The agglutination was stable when the drug was injected intravenously into dogs and transient and unstable when the drug acted on the blood in the test tube. The authors feel that three features of the pattern of development of the positive Coombs test in these experiments militate against an antigen-antibody interpretation, and emphasize the weakness of this hypothesis as a general explanation for all instances of positive Coombs' test. First, the rapid appearance of the positive Coombs test, within two days after injection of the drug, constitutes a strong objection to an antigen-antibody response. Second, the short-lived state of the positive test, as indicated by its disappearance in two to four weeks, is such as to be unusual for an antibody response. Finally, the lack of potentiation of the test by subsequent doses of the drug and the seemingly stereotyped response to subsequent doses do not connote immunologic characteristics. Phenylhydrazine is known to produce direct injury to erythrocytes, which is associated not only with hemolysis but also with alterations within the erythrocytes, as demonstrated by the production of methemoglobin and Heinz bodies. The pattern of observations suggests that phenylhydrazine alters the red blood cells in such manner as to change their capacity to react with the canine serum antiserum of the rabbit. The positive direct Coombs test appears to result from an alteration of the erythrocyte by phenylhydrazine or some breakdown product of phenylhydrazine.

Sudden and Unexpected Death Due to Disease. A. R. Moritz. GP **10**:35-42 (Dec.) 1954 [Kansas City, Mo.].

Sudden deaths from clinically unexplained causes constituted 12% of the total deaths in a large urban community. No age period was exempt, and the number of sudden deaths in each age group tended to be proportional to the total number of people of that age who died. Injuries can produce either instantaneous or delayed death without leaving external evidence. Moritz feels that in any locality where sudden deaths are certified as being due to disease, without the benefit of postmortem examination, a significant number of homicides, suicides, and fatal accidents pass unrecognized. The impact of a flat, padded object against a part of the head protected by hair or a cap or hat often causes fatal intracranial bleeding without leaving a visible or palpable lesion of the scalp. Although such a head injury may be almost immediately fatal, an interval of hours or even days may intervene between it and death. Injuries to the spinal cord with immediate death from spinal shock are observed without external evidence of injury. An impact against the thorax may be rapidly fatal either as a result of internal bleeding due to the rupture of the heart, lungs, liver or spleen, or as a result of laceration of the lungs or air passages. Blunt injuries of the abdomen may cause death within a few minutes from hemorrhage, or after hours or days as a result of shock or infection. The physician called to see a person whose death was sudden or unexplained should be alert to inconspicuous and easily overlooked penetrating wounds located within the external orifices. Poisoning is always a possibility in the event of death from unexplained causes. Not all fatal poisoning results in death by the mechanism of circulatory failure. Alcohol and barbiturates act principally on the central nervous system. It is often found that the person who died of arteriosclerotic heart disease had previously complained of periodic attacks of abdominal or thoracic pain, of shortness of breath, or of fainting spells. Many persons whose unexpected death was due to intracranial hemorrhage had previously complained of symptoms attributable to high blood pressure or of previous episodes of cerebral hemorrhage. In many instances of fatal coronary insufficiency postmortem examination fails to disclose occlusion of any major coronary artery. Coronary atherosclerosis, particularly in young adults, is frequently segmental, and the segment occluded by thrombus may be limited. In an illustration the author shows a recent thrombotic occlusion of a severely diseased segment of the left coronary artery of a man 28 years of age in whom death occurred unexpectedly. The disease of his coronary arteries was confined to a segment measuring less than 4 mm. in length. Any infection in which the organism gains access to the blood stream may run a rapidly fatal course (less than 24 hours). The intracranial diseases most commonly responsible for sudden death are those that result in hemorrhage. These lesions include berry aneurysms of the circle of Willis or its branches, hypertensive cerebrovascular disease, and gliomas. Suddenly developing edema in the vicinity of a clinically unsuspected brain tumor may cause unexpected collapse and death independently of hemorrhage. The author studied over 1,000 sudden deaths of apparently healthy young adults and found that complete autopsies failed to disclose an adequate cause of death in about 10%.

Mortality from Thyroid Diseases in an Endemic Goiter Area: Studies in Finland. E. A. Saxén and L. O. Saxén. Docum. med. geog. et trop. **6**:335-341 (Dec.) 1954 [Amsterdam, Netherlands].

The view that all adenomatous thyroid glands have significant malignant potentialities continues to gain support. Finland has areas in which goiter is endemic, but goiter is comparatively rare in regions of Finland with conditions that favor the presence of larger quantities of iodine. It has also been shown that the urine collected from persons living in areas where goiter is rare contains more iodine than that collected from persons in endemic areas. It should be remembered, however, that many factors influence the incidence of simple goiter. The most prominent feature of endemic goiter in Finland is the high incidence of adenoma and the relatively frequent occurrence of thyrotoxicosis. During the 16-year period from 1936 to 1950, inclusive, thyroid disease was the primary cause of death in 833 cases. The diagnosis of thyroid cancer was made in 137 cases and that of malignant goiter in 118. Thus, together they form about one-third of the cases in which thyroid disease was the cause of death. Further analysis revealed that the frequency of deaths from toxic goiter seems to follow that of goiter. The deaths due to exophthalmic goiter and malignant goiter also were perhaps more frequent in areas of endemic goiter but not sig-

nificantly so. The frequency of deaths from thyroid cancer seemed to have no correlation at all with the distribution of goiter. Thus, the geographical distribution of deaths from thyroid cancer does not support the hypothesis that goitrogenic factors are also carcinogenic. The fact that mortality from thyroid cancer does not significantly vary in different countries and that it seems to be even lower in countries where goiter is endemic also fails to support the hypothesis. However, it is known and has been shown in Finland that the frequency of different types of thyroid cancer varies in different areas and seems to be associated with variations in the incidence and type of goiter. The authors feel that the reported figures do not justify the radical view that, unless definitely contraindicated, all nodular goiters should be removed. However, indications for surgical removal of thyroid nodules may be different in endemic and nonendemic regions.

The Adenohypophysis and Hypothalamus in Hyperadrenalcorticalism. L. W. O'Neal and P. Heinbecker. Ann. Surg. 14:1-9 (Jan.) 1955 [Philadelphia].

Sections of the pituitary and of the hypothalamus were made in the course of autopsies carried out in two cases of adrenal cortical hyperfunction (Cushing's syndrome) in a 29-year-old woman with bilateral adrenal cortical hyperplasia and in a 58-year-old woman with adrenal cortical carcinoma. No microscopic or anatomic variations from the normal were observed in the hypothalamus of the patient with adrenal cortical hyperplasia; a basophilic adenoma was found in the anterior portion of the adenohypophysis and some of the basophils of which it was composed were typically hyalinized. Outside of the adenoma, all basophils were hyalinized. The hypothalamus also was normal in the case of the woman with adrenal cortical carcinoma; the pituitary exhibited no adenoma, but there was an increase in basophils, a high incidence of Crooke's cells, and a lower than normal acidophil count. Two clinical cases of adrenal cortical hyperfunction are described in a 36-year-old woman and a 43-year-old woman respectively. The younger woman had a mixed Cushing's-adrenogenital syndrome. The masculinization, hirsutism, hypertrophied clitoris, and increased 17-ketosteroid excretion were the prominent "adrenogenital" features. Polycythemia, hypertension, moonface and buffalo hump were the characteristic findings in the other patient. A left adrenal tumor was found on exploration and was removed in the first patient. Nine months after the surgical intervention she had lost 40 pounds; she no longer had moonface, plethora, or hypertension. A left subtotal adrenalectomy was performed in the other patient; one year after operation she was in good health, normotensive, and had a normal fasting blood sugar. These two cases illustrate that the symptoms of hyperadrenalcorticalism, whether due to cortical tumor or to cortical hyperplasia, are relieved by adequate adrenal surgery. Pituitaries of nine patients with various diseases such as lupus erythematosus, hypertensive encephalopathy, chronic lymphatic leukemia, agranulocytosis, acute leukemia, and thrombocytopenic purpura, who received cortisone or corticotropin (ACTH) for variable periods of time, were obtained from routine autopsy material. Postmortem examinations were done within 12 hours of death. The most common alterations in the pituitary in these cases was a statistically significant increase in the relative number of basophils, with or without hyalinization of their cytoplasm. Typical Crooke's cells were numerous in the pituitaries of two patients who had received cortisone for six months but were infrequent in the pituitary of a woman who had received cortisone for almost a year but had not received any in the eight days before her death. In four patients no Crooke's cells were found, but in all patients dying while receiving cortisone, the basophils, whether hyalinized or not, exhibited darkstaining cytoplasm, with scanty granulation and often clear vacuoles. In several of the pituitaries there were focal nodular collections of cells composed entirely of basophils, especially in the anterior portion of the adenohypophysis. Adrenal cortical hyperfunction appears to be associated with: (1) hormonal secretion arising in an adrenal cortical adenoma or carcinoma that probably is not under adenohypophyseal control, (2) adrenal cortical hyperplasia and overactivity. The stimulus for the cortical hyperplasia is presumably increased secretion of corticotropin (ACTH) by the pituitary. This concept indicates only the participation of the pituitary, not necessarily its primacy. The study of the pituitaries in patients with adrenal cortical hyperfunction and in the patients treated with cortisone failed to yield conclusive evidence as to the cell of origin of corticotropin. Since basophil hyperplasia and hyalinized basophil cells were seen in the pituitaries of the patients treated with cortisone, the Crooke's cells are secondary to hyperadrenalcorticalism and cannot be considered to be primary in the pathogenesis of adrenal cortical hyperfunction. The significance of the Crooke's cells remains obscure. The occurrence of nodular hyperplasia of the basophils following cortisone administration raises the possibility that some of the "basophil adenomas" in adrenal cortical hyperfunction are not true neoplasms but represent nodular hyperplasia secondary to hypercorticalism. Since microscopic examination of the hypothalamus revealed normal tissues in the presence of adrenal cortical hyperfunction associated with adrenal hyperplasia, degenerative changes in the paraventricular nuclei cannot be considered to be the sole primary pathogenic lesion in this condition.

Clot Culture in Typhoid Fever. K. C. Watson. J. Clin. Path. 7:305-307 (Nov.) 1954 [London, England].

Watson points out that in the early diagnosis of typhoid fever the emphasis has for long been on the isolation of Salmonella typhi from blood culture. Clot culture techniques have not enjoyed the same vogue, although Felix had found in 1924 that clot culture was hardly ever unsuccessful if blood culture was successful but that the reverse was frequently true. Watson calls attention to investigations carried out by himself and associates in which streptokinase bile broth (containing 100 units per ml. of streptokinase) had proved highly effective as a culture medium for blood clot. Experiences with this method since then bore out, the initial favorable results, and, as a result of its application, it soon became apparent that the results of clot culture were considerably better than those of blood culture. In one series of 99 cases since the introduction of streptokinase there were 48 positive blood cultures and 93 positive clot cultures. Two possibilities arose that might be responsible for these results: (1) streptokinase might exert a specific stimulating effect on the growth of S. typhi, or (2) removal of the serum before culturing the clot might increase the chances of obtaining a positive isolation. The action of streptokinase appears to be purely an enzyme one concerned with fibrinolysis. In this paper studies are described of the effect of serum factors on the isolation of S. typhi from blood clot and whole blood. It was found that 11 of 28 half-clots incubated with serum gave a negative result, whereas all 28 half-clots incubated without serum were positive. Since these were corresponding halves of the same clots, it is improbable that the former were initially sterile. In further studies on serum factors in blood cultures, Watson proved that bactericidal serum factors may exist in sufficient concentration to militate against successful isolation of S. typhi when the volume of medium is too small. No correlation between the bactericidal action of serum and the level of circulating agglutinins was found. The bactericidal action of serum on S. typhi is dependent on the strain of organisms as well as on the serum.

Observations on the Female Sex Chromatin in Human Epidermis and on the Value of Skin Biopsy in Determining Sex. J. L. Emery and M. McMillan. J. Path. & Bact. 68:17-22 (July) 1954 [Edinburgh, Sotland].

Emery and McMillan point out that Barr and Bertram in 1948 first noticed a chromatin body about 1 μ in diameter lying adjacent to the large nucleolus in nerve cells of a cat, an observation that led to the discovery that this distinctive nuclear form was related to the sex of the animal. The chromatin mass, which was first called "nucleolar satellite" and later "sex chromatin," was seen to be considerably larger in females than in males. Graham and Barr demonstrated in 1952 that this sex difference in nuclear morphology occurs in cells of smooth, skeletal, and cardiac muscle; in cartilage, epidermis, endothelium, kidney, thymus, adrenal cortex and medulla; and in several types of glandular epithelium. In the nuclei of cells other than neurones, the sex chromatin appears as a plano-

convex body flattened against the nuclear membrane. Like other chromatin, it stains well with basic dyes. Emery and McMillan describe their studies on three groups of skin sections: 54 sections were obtained by biopsy from children, 55 from newborn infants post mortem, and 10 from adult patients by biopsy. Their observations largely confirm the claims made by Barr and his colleagues that sex can be determined from the examination of skin sections. It would seem possible that a correct determination of sex could be carried out on skin obtained post mortem in about 8 out of 10 cases, and in the rest an equivocal but not erroneous result would be obtained. The skin biopsy method of sex determination promises to be of value in three fields. First, in cases of pseudohermaphroditism, in which it can eliminate the need for laparotomy and obviate the removal of gonadal tissue for a histological decision. Second, in medicolegal cases, in which, if postmortem changes are not too advanced, it might be possible to suggest the sex from a fragment of skin. Third, since the sex chromatin is visible in many tissues of the body and in the cells of certain tumors, academic interest attaches to the determination of the chromosomal sex in the tissues of teratomatous or gonadotrophin-producing tumors in males.

RADIOLOGY

Some Observations Concerned with Carcinoma of the Breast: Part III. M. W. Miller and E. P. Pendergrass. Am. J. Roentgenol. **72:**942-952 (Dec.) 1954 [Springfield, Ill.].

Part 1 of this investigation (abstracted in *J. A. M. A.* **156:**1203 [Nov. 20] 1954) included the statistics of survival for 1,029 patients treated by operation and/or irradiation. Part 2 (abstracted in *J. A. M. A.* **156:**1292 [Nov. 27] 1954) included the results of radiation treatment combined with operation. The present report is concerned with an analysis of irradiation for recurrences or metastases, the effect of castration, and the effect of the size of the original tumor on survivals. In 1,034 patients with carcinoma of the breast seen at the Hospital of the University of Pennsylvania between 1923 and 1943, of which group 1,029 cases were coded, there were 423 who had local recurrences, of which number 390 either had concurrent or later metastases. Of the 606 not having local recurrences, 359 had concurrent or later metastases. The 256 patients having local recurrences treated by surgery or irradiation had a 25% five year survival. The 167 patients having local recurrences not treated by surgery or irradiation had a 22.6% five year survival. The 432 patients recorded as having metastases treated by irradiation had a 21.2% five year survival, while the 317 patients recorded as having metastases not treated by irradiation had a 19.2% five year survival. The tumor dose of roentgen rays or radium used for local recurrences and/or metastases was in most instances less than 3,000 r and usually resulted in slight to marked regression of the local lesion. The 280 patients recorded as not having metastases had a 76% five year survival. The 336 patients not having reached the menopause had a 39.8% five year survival, and the 460 having reached the menopause (naturally or by castration) had a 34.1% five year survival. The 214 patients not having menopausal history recorded had a 34.5% five year survival. The 74 patients having castration performed after the diagnosis of breast cancer showed a 33.7% five year survival. In 53 castrated for recurrences or metastases, there was a beneficial effect on the local lesion in 18 patients. The original tumors ranged in size from less than 20 to over 90 mm. Five year survival decreased directly as the size of the tumor increased, that is, the larger the tumor the worse the prognosis.

The Rationale and Results of Simple Mastectomy plus Radiotherapy in Primary Cancer of the Breast. L. H. Garland. Am. J. Roentgenol. **72:**923-941 (Dec.) 1954 [Springfield, Ill.].

Garland points out that the problem of cancer of the breast is fundamentally the problem of cancer outside the breast. When the disease is confined to the breast itself, simple mastectomy alone will cure. In strictly localized or biologically favorable cases simple excision of the tumor will cure. When the disease has spread beyond the breast, radical mastectomy of the Halsted type will cure only in that group of cases in which the spread is still confined to the removable tissues of the chest wall and axilla. Data on long-term survival rates, and recent observations on the frequency of internal mammary lymph node involvement, indicate that this "locally confined" group with extramammary involvement is relatively small, being about 10% of all patients admitted with primary tumors. In 100 consecutive women with primary cancer of the breast, some will have apparently operable cancer when first seen, some questionably operable, and some frankly inoperable. The proportions naturally vary, but in most reported series, about 60% of cases fall into the first or apparently operable group, and about 40% into the other two groups. In the operable group, radical surgery results in some 80% five year survivals when the axillary lymph nodes are not yet involved and in about 30% of five year survivals when there is such involvement. Radical surgery is contraindicated in most of the questionably operable and in all of the frankly inoperable cases. It may hasten the spread of fresh cancer emboli throughout the chest wall and body, and will actually shorten survival time in some patients. There are about 11 out of 100 cases in which the radical operation is of significant value in terms of survival. Adequate postoperative radiotherapy (about 4,000 r, tissue, in 15 to 21 days) will do more for the axillary lymph nodes in those members of this group with radiosensitive lesions than will radical dissection of the axilla. It will not spread neoplastic cells; it should destroy or suppress tumor. Conversely, radical dissection will do more for those members of the group with radioresistant lesions. The question therefore is, what is the proportion of radiosensitive and radioresistant tumors in this hypothetical group of 11 patients? Since the radiosensitivity of lesions is not determinable prior to treatment, and, since surgical removal is a more certain method of eradicating a localized (i. e., removable) breast cancer than is radiotherapy, it is advisable that surgery be used to remove the primary lesion in all apparently operable cases. The radical procedure is preferable to the simple operation in a special group of patients with operable lesions (the very obese woman, the one with apical tuberculosis, and the unstable person who will probably fail to complete her postoperative therapy course). It is possible that light-complexioned women under 50 years of age, with clinically favorable tumors (i. e., of slow growth rate, apparently locally confined and therefore potentially well differentiated or radioresistant) also should have radical operation in preference to vigorous radiotherapy. Patients with presumed internal mammary lymph node involvement (especially those with central or inner quadrant tumors) probably should have additional radiotherapy to this area. Garland concludes that the place of simple mastectomy and vigorous postoperative radiotherapy in the treatment of primary operable cancer of the breast appears to be well established and that it is the method of choice in most cases, provided skilled radiotherapeutic service is available. The physical comfort of the average woman treated by simple operation and postoperative radiotherapy appears to be greater than after the radical procedure. Either method still fails to cure a majority of women with breast cancer today.

Large Doses of I^{131} in Dogs: Radiation Dosage Correlated with Histologic and Autoradiographic Changes. M. B. Levene, G. A. Andrews and R. M. Kniseley. Am. J. Roentgenol. **73:**88-97 (Jan.) 1955 [Springfield, Ill.].

Reports on pathological changes in human thyroid tissue after large doses of I^{131} have emphasized the variability of response. Most experimental studies have been made in small laboratory animals, but since the distribution of ionization produced by I^{131} is dependent on the volume and dimensions of the thyroid, observations on larger animals should be more informative. This report is concerned with studies on 8 dogs weighing from 10 to 15.7 kg. These dogs were given 1.5 mc. of I^{131} per kilogram. Urine collections were made daily, and venous blood samples were also obtained daily. Radioactivity over the thyroid region was ascertained each day by means of a collimated Geiger tube. On the 3rd, 4th, 5th, 6th, 9th, 12th, 20th, and 31st days after administration of the I^{131}, one animal was

killed. The thyroids, parathyroids, and an adjacent section of trachea were removed from each dog. Immediately after removal each pair of thyroids was assayed with both the collimated Geiger tube and a Lauritsen electroscope. The glands were then weighed and blocks were cut and were fixed for subsequent histological and autoradiographic preparation. During the period between injection and killing there was little departure from normal in the clinical behavior of the animals. A distinct time pattern of histopathological changes was found, with morphological evidence of inflammation and necrosis developing after the third day. Destruction of the gland was correlated with release of I^{131} from the thyroid into the blood stream. A patchy rim of preserved follicles was seen in the animals killed on the sixth and ninth days, and these follicles were shown by autoradiographic studies to have retained the radioisotope selectively. At later intervals necrosis was complete, and autoradiographs showed focal zones of radioactivity. It is believed that the important differences at the various intervals after administration are related chiefly to the time required for development of morphological evidence of inflammation and necrosis, rather than to the higher dosages in the animals killed at later times. The authors believe that if all the radioactivity could have been removed from the glands after three days when there was no demonstrable histological effect, the sequence of later changes would have been essentially the same as those seen. Published reports suggest that this sequence of events occurs more rapidly in rats and mice than in dogs, and the authors say that their experience indicates that it occurs even more slowly in human beings. The factors influencing the distribution of histopathological necrosis in the thyroid gland are obviously complex and poorly understood. It is the opinion of the authors that the most important single explanation for the subcapsular groups of preserved follicles is the lack of cross fire to these follicles from beta particles.

Functional Restoration of the Shoulder by Deep X-ray Therapy in Bursitis. L. J. Gelber. New York J. Med. **54:**2971-2975 (Nov. 1) 1954 [New York].

Deep x-ray treatment was given to 435 patients with subdeltoid and subacromial bursitis between 1945 and 1953. The most characteristic symptom was pain and limited motility. Treatment consisted of 8 to 10 applications of 200 r each in air, 50 cm. distance, with a filtration factor of 0.5 mm. Cu—1 mm. Al, with 200 kv. (peak). A total dose of 600 r was applied anteriorly, 300 posteriorly, and 200 to 300 laterally over the bursal region, until there was complete restoration of function. Treatments were spaced four times a week until a total of 1,000 to 1,200 r was given. As a rule, pain was relieved after the second or third treatment. In chronic cases a higher total dosage, 1,200 to 1,500 r may have to be given, because much more damage has occurred to the bursa. Successful therapy depends first on thorough treatment of the bursitis and second on treating such complications as frozen shoulder, arthritis, and cervicobrachial radiculitis, if present. It is essential to continue to treat all patients with bursitis with deep therapy until motion is completely restored and no tenderness whatsoever exists about the shoulder joint. There are recurrences if patients are dismissed too early. Preservation of skin tone with Rayderm Ointment (containing antihistamine) proved satisfactory for the care of the irradiated skin during roentgen therapy.

Obesity and Hypophysial Roentgen Therapy. R. Nadal, M. Nel and A. Ravina. Presse méd. **62:**1664-1667 (Dec. 1) 1954 (In French) [Paris, France].

Three cases of obesity in women are described. Two resulted from emotional conflicts and were accompanied by amenorrhea and headache; one case was also accompanied by anorexia and an anxiety neurosis. The third case occurred post partum and was repeated after two further pregnancies. All three patients benefited to a greater or lesser extent from hypophysial roentgen irradiation. The authors discuss the various mechanisms involved in obesity and state that it is a disease having both exogenous and endogenous causes, though a given case does not necessarily include both. Roentgen treatment is given with 200 kv. tension and 1 Cu—2 mm. Al filtration. The routes used are the bitemporal, transmaxillary, and submaxillary. The frontal route is not advisable. The total dose is about 3,000 r in 20 applications (three per week). The treatment may be repeated three months later. The principal indications for this treatment are adrenal cortical hyperfunction (Cushing's disease) of hypophysial origin, postpartum spongious obesity, certain hypergonadal obesities occurring at periods of importance in genital life, and cases in which a functional or organic disturbance of the diencephalon has been proved.

Aortography in Clinical Diagnosis. S. Schorr, S. Z. Rosenberg and K. Braun. Harefuah **47:**223-225 (Dec. 1) 1954 (In Hebrew with English and French summaries) [Jerusalem-Tel Aviv, Israel].

Of 45 patients in whom aortography was performed, the percutaneous retrograde femoral route was used in 36, the percutaneous retrograde brachial route in 4, and the direct translumbar route in 5. Aortography is not without danger. The risk, however, can be minimized by the proper selection of cases and great care in the technique. Aortography should only be done in cases in which it is necessary to make or to confirm a diagnosis on which adequate treatment depends. The procedure is of value in the diagnosis of arterial obstruction, Leriche's syndrome, aneurysm of the thoracic and abdominal aorta, coarctation of the aorta, and in the diagnosis of anomalies of the renal arteries. It is an auxiliary diagnostic procedure in urologic conditions such as ureteral obstruction associated with a nonfunctioning kidney and cases of renal and adrenal tumors. By demonstrating the renal blood flow, aortography permits the study of both physiological and anatomic changes in the kidney in patients in whom intravenous pyelograms are unsatisfactory and retrograde pyelography not advisable. The same precautions used in the performance of intravenous pyelography should be observed in aortography. Technical improvements, such as rapid automatic changing of films and safer contrast mediums, will give further impetus to this diagnostic procedure. The authors prefer percutaneous retrograde femoral artery aortography with the Seldinger needle and catheter to the translumbar route. This method appears to be both safer and simpler. Thromboses, infections, or major hemorrhages did not occur after its use, and it yielded satisfactory results in most patients. Since the injection is made against the blood flow in the aorta, the flow of the contrast medium is slowed down and only small volumes of the medium are required (15 to 18 cc. of 70% concentrated iodopyracet [Diodrast] solution or sodium acetrizoate [Urokon Sodium]) for different positions. Since the polyethylene catheter may be left in situ for long periods, the diagnostic study may be more comprehensive and complete. Selective thoracic or abdominal aortography may be performed by adjusting properly the level of the tip of the catheter in the aorta. The direct translumbar route cannot be used to demonstrate the thoracic aorta. For this purpose the femoral or brachial artery was used.

PHYSIOLOGY

Number and Distribution of Human Hemic Cells. E. E. Osgood. Blood **9:**1141-1154 (Dec.) 1954 [New York].

Methods are described that make possible the calculation of the total number of each type of the hemic cells of the body and their distribution in the hematopoietic organs, the blood, and outside the blood and the blood-forming organs. The numbers of the hemic cells according to this distribution and in the total body are summarized in a table, together with the ratios of the number in the blood to the number outside the hematopoietic organs for standard man, the 154 lb. (70 kg.) human male. Dividing these figures by 70 will give the values per kilogram. By similar methods the values for other age and sex groups in man and for other species may be calculated. Leukocytes apparently are not primarily blood cells but are merely on their way in the blood to the defense of body tissue generally. Only one-fortieth to one four-hundredth of the total leukocytes outside the hematopoietic organs are present in the blood stream at any

one time. These somewhat surprising figures account for many previously made observations which were hitherto hard to explain.

Experimental Study of Induced Hypothermia. R. de Vernejoul, H. Metras, P. Ottavioli and others. Presse méd. **62**:1679-1680 (Dec. 4) 1954 (In French) [Paris, France].

The effects of hypothermia were studied in 29 dogs: 15 of them were cooled internally, i. e., through the bloodstream, and 5 externally by immersion into cold water. The remaining nine dogs were used to study various single points, such as coronary, urinary, and cerebral output. Oxygen consumption was rapidly lowered along with temperature but never reached a point at which it was negligible, contrary to the opinion of some authors. The hemoglobin oxygen saturation decreased slightly with the temperature, although the dogs were in pure oxygen during the experiments. There was a decrease in coronary flow when the venae cavae of one dog were ligated; cardiac arrest occurred in this case after 12 minutes of clamping. The oxygen consumption of the brain paralleled that of other tissues; this shows the danger of anoxemia even at low temperatures. Of the 15 animals which had internal refrigeration only 7 survived the whole procedure more than 24 hours, while one died of cerebral anoxia, one of hemorrhage due to heparin administration, and the other 6 of ventricular fibrillation or secondary thrombosis. Of the five which had external refrigeration, one died of irreversible ventricular fibrillation. The authors favor external cooling. The problems involved in hypothermia as an adjuvant to intracardiac surgery resolve themselves into three categories: hemorrhage, cerebral and myocardial anoxia, and shock due to blood denaturation. The authors studied the effect of cold on plasma proteins by repeated electrophoreses during the experiments. They noted that when an animal went into shock an increase in its gamma globulins occurred. In cases in which a dog died within 24 hours of the induction of hypothermia, the alpha globulins were seen to increase by 100% or more. No modifications in the electrocardiogram accompanied these phenomena, so they may well represent responses of the plasma proteins to cold.

Aldosterone, a New Adrenal Cortical Steroid. L. de Gennes and G. Deltour. Presse méd. **62**:1751-1752 (Dec. 18) 1954 (In French) [Paris, France].

Aldosterone (electrocortine [Δ 4-pregnene-3,20-diceto-11β,21-dihydroxy-18-AL]), isolated by Simpson and co-workers, appears to be an answer to the much-discussed "hormone of water and salt." Although it is probably not the only one of that nature, the hormone appears to have properties qualitatively similar to those of desoxycorticosterone, which has never been proved to be a natural hormone. Aldosterone shows effects of glyconeogenesis that indicate that it is a steroid having all the principal properties of adrenal cortical secretion, if not all the action of the adrenal cortex on electrolyte metabolism. Its effect in minute doses in experimental animals suggests that it may be the agent of choice in adrenal cortical replacement therapy. Its role in electrolyte balance, particularly in regard to sodium and potassium, should clarify the physiopathology of a number of conditions in which the regulating factor of water and salt seems to be incriminated, but the nature and mode of action of this factor are not clear.

Comparison of Effects of Intra-Arterial and Intravenous Transfusions in Hemorrhagic Hypotension on Coronary Blood Flow, Systemic Blood Pressure and Ventricular End Diastolic Pressure. E. O. Theilen, M. H. Paul and D. E. Gregg. J. Appl. Physiol. **7**:248-252 (Nov.) 1954 [Washington, D. C.].

The preferential use of the intra-arterial route in acute severe hemorrhagic shock has been proposed by some on the assumptions that (1) intra-arterial transfusion produces a more rapid increase in systemic pressure as a result of a hydraulic effect; (2) perfusion of the coronary bed is more quickly and effectively reestablished, thus favoring the improvement of myocardial function; and (3) a larger volume of blood can be transfused by the intra-arterial route without producing dangerous elevations of venous blood pressure and right ventricular dilatation. Theilen and associates describe experiments that were devised to evaluate the relative hemodynamic responses in experimental hypotension due to hemorrhage to each of these two routes of blood administration. The experiments were made on mongrel dogs weighing 11 to 22 kg. (24.5 to 48.5 lb.). Pressure determinations were made from the carotid artery, right ventricle, and left ventricle. After cannulation of the coronary artery and after a control record had been obtained, the animal was bled rapidly from the femoral artery to a pressure level in the femoral artery that ranged from 5 to 57 mm. Hg in different dogs. A given pressure level was then maintained by further bleeding or reinfusion until the blood pressure had stabilized at the desired level. This period of time at a stable hypotensive level varied from 5 to 40 minutes and averaged 17 minutes. The withdrawn blood was then reinfused at a rate of 50 to 100 ml. per minute; this rate would be comparable to about 250 to 450 ml. per minute in a 70 kg. (154.5 lb.) man. Insofar as possible, each animal served as its own control; alternate transfusions were given by the arterial and venous routes in equal volume and at equal rates. In a series of 12 animals the two routes of transfusion were equally effective in restoring systemic pressure and coronary flow. With the infusion rates used, excessive elevations of right ventricular end diastolic pressure or evidence of acute myocardial failure did not occur. Thus it appears that in these dogs with hypotension of varying degrees of severity but of relatively short duration intra-arterial transfusion is no more effective than intravenous transfusion with respect to restoration of coronary blood flow.

Secular Progression of Human Stature. H. Günther. München. med. Wchnschr. **96**:1411-1414 (Nov. 26) 1954 [Munich, Germany].

By secular progression in stature Günther means the increase in height that took place during the last century. The steady increase in human stature that has been taking place in the course of the 18th and 19th century is an established fact, for which as yet no satisfactory explanation has been found. A possible connection with the increasing process of civilization has yet to be proved, since variations in stature among the less highly civilized peoples have yet to be demonstrated. Explanations that consider changes in external conditions (mode of living, nutrition, and other factors) are unsatisfactory. The steady changes in the growth process suggest a modification in the regulatory mechanisms, presumably mostly in hormonal regulations. Approaching this problem from various angles, one realizes a steady change in human constitution, particularly in the endocrine system. A deeper insight into this problem, however, is still not possible. The question is not merely an anthropological one, it is also a medical problem because of changes in constitution. Circulatory changes may be expected, and some are already evident. In an earlier report on this problem the author plotted curves on the progression in stature of 20-year-old males. A century ago maximum height had not yet been reached at this age, for during the last century not only has the stature increased but growth has also been accelerated, so that now full growth is often reached at the age of 20 or earlier. Linear progression of human stature has been demonstrated only during the last century. It does not go back unrestrictedly to earlier centuries, because if this were so, men of the 15th century would have been almost dwarfs, which is not in keeping with reality. Although it has been pointed out that medieval armor is too small for persons of average size today, centuries before that human stature was not much smaller. The author believes that the secular linear progression of stature probably began after 1830. He comments on the possible role of factors such as living conditions, diet (increase in meat consumption), increasing urbanization, and on changes in the combination of genes as the result of more mixing among different peoples, particularly in countries like the United States. He also mentions the opinion of some scientists, Depéret, for instance, that there is a general tendency toward increased size in all species, and that this would ultimately lead to degeneration. The dying out of species that have reached maximum size is the termination of phylogenetic development.

BOOK REVIEWS

Diseases Transmitted from Animals to Man. By Thomas G. Hull, Ph.D., Secretary, Council on Scientific Assembly, American Medical Association, Chicago. Contributors: Charles Armstrong, M.D., et al. Fourth edition. Cloth. $12.50. Pp. 717, with 104 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Board St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, Canada, 1955.

This book deals with diseases of vertebrate animals transmissible to man. It does not include diseases of men for which there is a reservoir of the infective agent in animals with an inapparent infection or the poisoning of man by toxins or venoms normally present in fish or snakes. It is eight years since the publication of the third edition of this book, and many changes have been made. New chapters not in the last edition cover vibrio abortion, vesicular stomatitis, Newcastle disease, regional lymphadenitis, pseudotuberculosis, hemorrhagic septicemia, and rickettsialpox. The chapter on foot-and-mouth disease has been omitted, and certain other chapters have been combined under new headings. The list of contributors has been increased, and the author of each chapter is named, which is an improvement over the third edition in which the authors were only mentioned in a footnote and those chapters prepared by Dr. Hull carried no credit line. Although one of the contributors, Dr. Kelser, has been dead for several years there is no indication of this in the book, and his chapter on rabies shows only minimal changes. In accordance with the change in the naming of the genus from Listerella to Listeria the name of the disease it causes is now listeriosis. Some of the old illustrations have been dropped, and many others have been added. This book continues to be an outstanding contribution to its subject and should be of great value to veterinarians, physicians, public health authorities, and research workers in the field of medicine and the ancillary sciences. Each chapter ends with a summary labeled "Items of Note" and an extensive list of references. Helpful tables are included. The index appears to be complete.

Diagnostic Laboratory Hematology. By George E. Cartwright, M.D., Associate Professor of Medicine, College of Medicine, University of Utah, Salt Lake City. Cloth. $3. Pp. 104, with 6 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1954.

This book, which is intended as a manual for medical students and practicing physicians alike, covers the various techniques used in hematological diagnosis and interpretations. It is, for the most part, based on the author's experience, which is both extensive and sound. Unfortunately, much ambivalence is occasionally manifested; in some areas the author gives only the sketchiest description, as in the discussion of the osmotic fragility test, whereas in other tests less commonly used, such as the determination of stool urobilinogen, the technique is given in great detail. By and large the description of the tests, with a commentary on their interpretation, pitfalls, and significance, is excellent. Some points which will provoke disagreement are the presentation of the Sahli method for hemoglobin determination as the method of choice; the suggestion that the B-D blade, kept in alcohol between finger punctures, should be used for obtaining capillary blood, without comment as to the danger of the transmission of homologous serum jaundice by this technique; the recommendation of the oxalate method for L. E. preparations when the clot technique is superior; the inclusion of a rather unsatisfactory technique of preparing marrow for examination; and the omission of a discussion of either paper or Tisselius electrophoresis. This is a good book, though its scope is quite limited. It brings together under one cover much finite information, yet fails on one hand to be thoroughly comprehensive and on the other hand to present material that cannot be readily found in general clinical laboratory manuals and good hematological texts.

Klinisch-röntgenologische Differentialdiagnostik der Lungenkrankheiten. Von Dr. Lasar Dünner, Chefarzt der Industrial Chest Diseases Clinic in Hull (England). Cloth. 49 marks. Pp. 274, with 334 illustrations. Ferdinand Enke, Hasenbergsteige 3, (14a) Stuttgart-W., Germany, 1954.

This text describes in didactic form the differential diagnosis of pulmonary diseases as observed over many years by the author and his colleagues. It presents the viewpoint of the internist, the lung specialist, the roentgenologist, and the pediatrician. It makes no claim to cover all differential diagnostic methods but only those with practical value. Unreliable and investigative details are briefly mentioned or omitted. It is not true that all diagnostic difficulties can be overcome. The personal element plays an important role in making a differential diagnosis. Some readers may find certain elements that they consider important lacking in the author's method. The inclusion of many excellent illustrations makes it easy for those with only a superficial knowledge of German to grasp most of the author's points.

Hugh Roy Cullen: A Story of American Opportunity. By Ed Kilman and Theon Wright. Cloth. $4. Pp. 376, with illustrations by Nick Eggenhoffer. Prentice-Hall, Inc., 70 Fifth Ave., New York City 11, 1954.

This biography is the true story of what honesty and hard work can do in a land that gives freedom to individual initiative. The story is a fine antidote for the defeatism that is attacking American youth and for the virus of dependence on getting "breaks" and "striking it rich." Mr. Cullen's early life was characterized by courage, integrity, and laudable self-confidence. He said, "I never tried to out-trade a man and I never let a man out-trade me." When men looked askance at some of the risks he took, they did not know the risks had been well calculated. He knew that "anybody can swim into a whirlpool but it's coming out of it that counts." Born in Denton County, Texas, in 1881, young Cullen had dreams of great things. As a struggling cotton broker, oil lease prospector, and finally, as an oil man on his own, he had the will and the drive to make his dreams come true. He was a young cotton broker in Oklahoma Territory when it became a state. He fought in some of Oklahoma's early political battles and was thereafter interested in political affairs. With possibly one exception, Mr. Cullen was the richest of the amazing Texans. He made nearly a billion dollars and gave away about 90% of it. Although much of it—perhaps most—went to the University of Houston, in two days he gave 4 million dollars to Houston hospitals. He gave generously for medical schools and research enterprises without which medical progress could not adequately go forward. This reviewer conceives of Mr. Cullen as being of a scientific turn of mind, because the University of Pittsburgh conferred on him the degree of doctor of science and because he gave so generously to institutions in which the teaching of science prevails. The book is well written and well illustrated. Americans in general and young Americans in particular should gain some expansion of mind and heart through reading the story of this generous Texan.

Pediatric Diagnosis. By Morris Green, M.D., Assistant Professor of Pediatrics, Yale University School of Medicine, New Haven, Conn., and Julius B. Richmond, M.D., Professor and Chairman of Department of Pediatrics, State University of New York College of Medicine, Syracuse. Cloth. $10. Pp. 436. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, England, 1954.

This textbook is unique in that it is just as important to the practitioner as to the student from the standpoint of increasing the skill of both by a systematic method for diagnosis and interpretation of physical findings. It is also unusual for a small

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

textbook of this type to cover so well the entire subject of pediatrics. The method of accurate history taking and physical examination, starting with the head and neck and continuing in detail through the various systems, is most effective and instructive. Symptoms referable to the various systems are also taken up in great detail. The coverage of growth and development and a section on health supervision are most interesting. This book is highly recommended for the teacher of pediatrics, the practitioner, and the medical student.

The Human Brain in Sagittal Section. By Marcus Singer, Ph.D., Professor of Zoology, Cornell University, Ithaca, N. Y., and Paul I. Yakovlev, M.D., Assistant Clinical Professor, Department of Neurology, Harvard Medical School, Boston. Publication number 228, American Lecture Series, monograph in American Lectures in Anatomy. Edited by Otto F. Kampmeier, Ph.D., M.D., Head of Department of Anatomy, School of Medicine, College of Medical Evangelists, Loma Linda, Calif. Cloth. $7.75; flexible binding $6.25. Pp. 81, with 46 plates. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, Canada, 1954.

The authors believe that sections of cerebral hemisphere cut in the sagittal plane, in place of the more usual frontal or horizontal cuttings, disclose the structural pattern of the neuraxis in a more satisfactory manner. This certainly holds for the principal nuclei of the brain stem and the course of the major fiber connections to the basal ganglia, as disclosed by the photographs of sections, 1.5 and 2.5 times actual size, reproduced in this atlas. Latin terminology has been used but a cross index includes English and other equivalents and popular synonyms. The brain used for these sections was from a healthy man, who died a short time after he fell and broke his neck. The sections selected for reproduction were stained with iron hematoxylin for myelin sheaths. Owing to technical difficulties, of either staining or photographing, the plates are somewhat uneven and in places blurred. The atlas should be useful to neuropathologists as a reference for hodological research, especially in the study of secondary degenerations after brain disease or injury and after surgical extirpations, such as leukotomies.

A Policy for Skilled Manpower. Statement by National Manpower Council with Facts and Issues prepared by research staff. Cloth. $4.50. Pp. 299. Columbia University Press, 2960 Broadway, New York 27, 1954.

The National Manpower Council was established in 1951 under a grant from the Ford Foundation. This volume has been preceded by three others, two of which dealt with scientific and professional personnel. This publication is concerned with manpower problems at the technical level and is applicable to the problems of recruitment, training, and use of technicians and skilled workers necessary for the provision of adequate health services. Part 1 of this volume incorporates the recommendations of the National Manpower Council directed toward the further development of resources of technical and skilled personnel and their more effective use. Part 2 is devoted to a more detailed study of facts and issues about skilled manpower, including trends in needs, general and vocational education, opportunities and incentives, and vocational guidance and counseling. The material is clearly presented and though of little general interest it should be of value to educators and administrators in all of the health fields.

Tumours of Lymphoid Tissue. By George Lumb, M.D., Consultant Pathologist, Westminster Hospital, London. Foreword by Sir Stanford Cade, K.B.E., C.B., D.Sc., Senior Surgeon, Westminster Hospital. Cloth. $8. Pp. 204, with illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Pl., Edinburgh 1, Scotland, 1954.

This monograph is based on studies of 140 patients with tumors of lymphoid tissues. Its 14 chapters discuss structure, function, and significance of lymphoid tissue; historical survey; terminology and classification, incidence of tumors of lymphoid tissue; follicular lymphoma; lymphosarcoma; reticular lymphoma; Hodgkin's disease; reticulum cell sarcoma; anaplastic sarcoma of lymphoid tissue; problems of diagnosis; effects of therapy on primary tumors of lymphoid tissue; general conclusions; and illustrative cases. The author has arranged the tumors of lymphoid tissue into (1) those having lymphocytic differentiation (lymphosarcomas that include lymphatic leukemia with lymph node involvement and follicular lymphomas); (2) those having reticulum cell differentiation—the reticulum cell sarcoma; (3) those with a mixture of cell types that include Hodgkin's disease and reticular lymphoma; and (4) those with imperfect development making impossible a cell-type differentiation. Lumb's account leaves little doubt that Hodgkin's disease is a cancerous growth. The monograph is recommended to pathologists and clinicians as a clear statement of present views on tumors of lymphoid tissues.

Angiopathia Diabetica: Konservative Behandlung des Zuckerbrandes. Von Prof. Dr. M. Bürger, Leipzig. Cloth. $16.40; 69 marks. Pp. 190, with 81 illustrations. Georg Thieme, Herdweg 63, (14a) Stuttgart, Germany; agents in U. S. A. and Canada, Intercontinental Medical Book Corporation, New York 16, 1954.

This monograph is largely concerned with vascular complications of diabetes. The author has had wide experience with gangrene, particularly. Since the management of diabetes with diet and insulin and the effects of work and exercise are carefully considered, especially in the second of the book's three sections, its title is somewhat misleading, but the possible relationships between therapy and blood vessel complications are discussed, even so. The title could well be adopted universally as a name for those vascular conditions that are peculiar to (and increasingly common in) diabetes mellitus now that insulin keeps diabetics living long enough to acquire them so frequently. From the mechanical and technical standpoints this book is beautifully conceived and executed, with glossy paper of fine quality, large page size, and many illustrations. Its generous number of tables and diagrams are well organized and clear. All students who are interested in the relationships between diabetes and angiopathy should have the benefit of this faithful record of rich experience in Leipzig.

The Epilepsies: Electro-Clinical Correlations. By Henri Gastaut, professeur à la Faculté de médecine de Marseille, Marseille, France. Translated by Mary A. B. Brazier, Neurophysiologist, Massachusetts General Hospital, Boston. With preface by Wilder Penfield. Publication number 204, American Lecture Series, monograph in Bannerstone division of American Lectures in Surgery. Edited by Michael E. De Bakey, M.D., Professor of Surgery and Chairman of Department of Surgery, Baylor University College of Medicine, Houston, Tex., and R. Glen Spurling, M.D., Clinical Professor of Surgery, University of Louisville, Louisville, Ky. Neurosurgery Division, editor: Barnes Woodhall, M.D., Professor of Neurosurgery, Duke Hospital, Durham, N. C. Cloth. $4.75. Pp. 149, with 20 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W. Toronto, 2B, Canada, 1954.

In his preface and in referring to local electrical discharges of the brain, Penfield states, "It is as though the epileptic process were providing a demonstration of the function of the various parts of the nervous system." As a faithful follower of Jackson and Penfield, Gastaut has written a brief book that attempts to answer the question in the mind of Jackson when confronted with each new patient: not "Is it epilepsy?" but "Where is the lesion that permits occasional excessive discharge?" To relate diverse clinical and electrical phenomena to anatomic localizations is an ambitious undertaking, which deserves a less compressed and staccato-like expression. Outline headings deal with clinical and electroencephalographic signs of epilepsy and physiological and pathological interpretation of each, the causes and the anatomic lesions of the epilepsies, and their diagnosis and treatment. Thirteen drawings and eight electroencephalogram reproductions illustrate the text. There are no bibliographical references. There is a detailed table of contents but no index. This small book lucidly explains laborious experiments and interprets the results logically. Nothing is lost in the translation. The treatise adds substantially to an understanding of the working of the human brain, and hence, deserves wide reading and study.

QUERIES AND MINOR NOTES

EXCESSIVE COFFEE DRINKING

TO THE EDITOR:—*Does drinking 20 to 30 cups of coffee daily definitely cause any harmful effects in any person?*

M.D., Connecticut.

This inquiry was referred to two consultants, whose respective replies follow—ED.

ANSWER.—Twenty to 30 cups of coffee contain a total of about 2 to 3 gm. of caffeine and considerable amounts of volatile coffee oil. The caffeine may cause nervousness, tremor, sensory disturbances (tinnitus, flashes of light), insomnia, headache, diuresis, tachycardia, and extrasystoles; the oil may cause digestive disturbances. In healthy persons these effects ordinarily are not serious and disappear promptly if the use of coffee is stopped. In persons with organic disease, such as cardiovascular, gastrointestinal or neural disease, however, these effects may be harmful, and the excessive use of coffee should be avoided.

ANSWER.—Any person who is obliged to inquire of his physician whether he is being harmfully affected by drinking 20 to 30 cups of coffee daily is surely not experiencing subjective evidences of deleterious action. Should he complain of tachycardia, palpitation, premature systoles, excessive perspiration, weakness, restlessness, and insomnia, one would suspect that these symptoms might be attributable to caffeine. Of the three xanthine derivatives of importance—caffeine, theobromine, and theophylline—there is more detailed knowledge of the action of theophylline on the cardiovascular system than of that of the other two, but it may be expected that they differ in their action from theophylline only quantitatively and not qualitatively. Theophylline causes generalized vasodilatation by direct relaxing action on vessel walls, including the coronary arteries; slows the heart through stimulation of the vagal nuclei in the medulla; opposes through central vasomotor stimulation the blood-pressure-lowering effect that would result from vascular dilatation; and directly stimulates the myocardium. The result of these diverse and opposing actions is usually an increase in cardiac output, which probably improves coronary circulation, because the coronary vessels are not affected by the central vasomotor stimulation.

There is animal and some human experimentation definitely establishing the fact that the xanthines increase the metabolism of skeletal muscle and that caffeine particularly sensitizes skeletal muscle with a resultant increase in response to stimulation. An increase in work output under the influence of caffeine has been established on the experimental level, and one might therefore expect that the ingestion of large amounts of the drug in the form of coffee would induce some weight loss providing the caloric intake was not stepped up proportionately. Caffeine is an inhibitor of cholinesterase and may affect chemical transmission from nerve to muscle, but such action would not likely be of direct clinical importance. Caffeine and the other xanthines increase gastric acidity, which could certainly be harmful in a person with peptic ulcer. These drugs also have a diuretic action, which may be due in part to increased renal blood flow accompanied by the lowering of renal venous pressure, although there is ample experimental evidence that the main action is a depression of tubular reabsorption. Increase is effected in sodium, potassium, chloride, and calcium excretion, the excretion of chloride being somewhat greater than that of sodium. However, even though the excessive coffee drinker may be obliged to urinate somewhat oftener than is usual, there is no evidence that this excessive urination is in itself harmful.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

DEGENERATIVE ARTHRITIS

TO THE EDITOR:—*A 41-year-old white structural iron worker was struck near the right knee by a 1,500 lb. beam that pushed the leg against a pile of iron. The injuries consisted of multiple superficial lacerations and abrasions of the right leg and a simple fracture of the upper third of the right fibula. Treatment consisted of dressing, crutches, and, later, hydrotherapy. The patient returned to work for one day, but two hours after beginning work he had pain in both knees, which grew worse, so he has been unable to return to work since because of pain in the knees. He also gets pains in the elbows, fingers, and muscles of the back. Examination is normal except for a limp due to voluntary fixation of the right knee and marked tenderness over both patellas and elbows without swelling. No real limitation of motion is present. On flexion of the knee with the examining hand held over the patella a grating is felt that causes pain for the patient. Routine laboratory tests, determination of sedimentation rate, prostatic smears, and roentgenograms of the joints involved are normal. The patient recently tried work again but lasted only three days. Can you suggest a diagnosis? Is it related to the previous injury?*

Paul R. Brother, M.D., Avenal, Calif.

ANSWER.—Since the patient has made two attempts to return to work and persisted for three days in the second attempt, it is assumed that his complaints are not of psychosomatic origin. The interval between the injury and the first attempt to return to work is not stated but is assumed to be several weeks. In general, return to such a strenuous occupation as that of a structural iron worker after several weeks of idleness might better have been preceded by a conditioning period at a lighter occupation or some extremely strenuous, general, postural-type exercises. The inquirer does not indicate that the pain occurring when the patient returned to work for the first time, which caused him to discontinue work, was any worse in one knee than the other. The subsequent pains in the elbows, fingers, and muscles in the back and the findings of tenderness over both patellas and elbows without swelling, pain and grating of the knee joints on flexion, and normal laboratory tests and roentgenograms all justify the conclusion that a generalized degenerative arthritic process must have existed for some time. It may be traumatic in origin and related to the patient's heavy work, or it may be due to the failure of, or decrease in, the anabolic processes related to repair of normal wear and tear within joints. Since the changes in the knees are rather advanced, this condition must have been going on to some degree before the injury and have been aggravated by the period of enforced idleness and the abnormal physiological factors incident to the injury.

So far as the general condition and health are concerned, the following recommendations are made as to medical treatment. 1. The patient should be given a high-protein, high-vitamin diet with extra vitamin B in the amount of about 100 mg. daily; extra ascorbic acid, 250 mg. to 500 mg. daily; and a multiple-vitamin capsule. 2. Adequate calcium intake should be insured by the use of calcium by mouth or two to three glasses of milk per day. 3. If there is any evidence whatever of gastric dysfunction or achlorhydria, the patient should be given accessory hydrochloric acid or glutamic acid hydrochloride (Acidulin) capsules to insure calcium absorption. 4. If there is any evidence whatever of thyroid deficiency, this should be corrected by administration of thyroid. 5. Since in the literature there is evidence that the steroid hormones are of significant importance in the anabolic processes carried on within the body, mixed steroid hormones such as a dose of both androgens and estrogens in proportions of 10:1 might be administered. Several preparations for oral medication are available consisting of 10 mg. of methyltestosterone with 1.25 mg. of estrogenic substance.

With regard to the knees, particularly the injured one, it is not stated whether there is instability in the knee joint or whether there is evidence of injury to the semilunar cartilages. The

patellar chondromalacia that is present, as indicated by the grating beneath the patellas, is, in itself, an indication of internal derangement of the knee and may be so advanced in the injured knee as to prevent restoration of normal function. The fact that the patient walks with "a limp due to voluntary fixation of the right knee" suggests some internal derangement in addition to the patellar chondromalacia. If such is the case it will have to be treated surgically; in any case, chondromalacia of the patella of an advanced degree would have to be attacked surgically. The exact operation to be performed on the patella is controversial at present and might consist of patellectomy, resection of the roughened surface of the patella with or without the addition of a fascial transplant, and restoration of the articular surface of the patella with a vitallium patellar prosthesis. This decision should be made by the operating surgeon. In answer to the specific questions, the suggested diagnosis is degenerative arthritis. It is probably related to the previous injury; at least, the injury constituted a marked aggravation.

BLOOD OF MARGINAL SINUS OF PLACENTA

To the Editor:—*An argument arose at one of our staff meetings as to the origin of the blood in the marginal sinus of the placenta. I said it was fetal on the basis of case reports I remembered of rupture of the marginal sinus with fetal death, presumably from blood loss. Please clarify.*

M.D., Michigan.

Answer.—The marginal sinus, according to Arey (Developmental Anatomy, ed. 4, Philadelphia, W. B. Saunders Company, 1940, p. 121), is an enlarged channel of varying extent that never completely encircles the margin of the placenta and through which some of the circulating fluid is drained from the placenta into maternal veins. Since the fetal and maternal vascular systems are separate, the origin of blood in the marginal sinus must be maternal. The loss of blood due to rupture of the sinus would, therefore, be maternal, and fetal death would be attributed to anoxia rather than to fetal hemorrhage.

SYPHILIS

To the Editor:—*A 54-year-old white man had syphilis in 1925 and was treated with arsenicals and bismuth over a two year period. In 1938 a Kolmer test of his blood, and a Wassermann test of his spinal fluid were negative, but his colloidal gold curve was 013322110000. In July, 1954, a Kolmer test of the spinal fluid showed a 4+ reaction with no cells, protein 17 mg. per 100 cc., and colloidal gold curve 001122210000. Because the patient was complaining of symptoms compatible with syphilitic involvement of the central nervous system, he was given 600,000 units of procaine penicillin daily for 14 days; three months later, a repeat lumbar puncture and Kolmer test showed a 4+ reaction, protein qualitatively zero and quantitatively 21.5 mg. per 100 cc., 2 lymphocytes, and a colloidal gold curve of 1233210000. Was therapy indicated in this case? Has it been adequate to assure against any future progression of the suspected disease of the central nervous system? Does the persistence of the positive reactions to the Kolmer test have any prognostic significance?*

J. Howard Latimer, M.D., Salt Lake City.

Answer.—The first point suggested by this query has to do with the validity of the laboratory report on the patient's spinal fluid in 1938, as compared with 1954. If these two spinal fluid examinations were made in the same laboratory, the laboratory may be regarded as unreliable, since it would be unusual almost to the point of impossibility that the complement fixation test in the spinal fluid, positive in 1954, should have been negative in 1938. Furthermore, a "4+ Kolmer" reaction in the spinal fluid cannot be definitely interpreted without knowledge of the dilutions of the spinal fluid with which the test was performed. The next point of importance is that the patient is stated to have been "complaining of symptoms compatible with syphilitic involvement of the central nervous system," but nothing is said of physical signs, and no indication is given as to what type of neurosyphilis the patient had or as to whether the same symptoms and signs were present in 1938. However, in general and for any type of neurosyphilis, 8,400,000 units of procaine penicillin within a 14 day period is probably adequate treatment. As to the adequacy of treatment, all patients with neurosyphilis should be given follow-up examinations at least at annual intervals for a minimum of five years after completion of treatment and at somewhat less frequent intervals after the first five years. The persistence of the positive reaction to the Kolmer test does not have any prognostic significance, since it may take a number of years for this sign to decrease in positivity after penicillin therapy or any other type of treatment.

TUBERCULOUS PREGNANT WOMEN

To the Editor:—*When* p-*aminosalicylic acid and isoniazid are given in therapeutic dosage to tuberculous pregnant women, what is the concentration of these drugs in the fetal blood? Is the fetus adversely affected by administration of these drugs to the mother?*

M.D., Sweden.

Answer.—Although it has been determined that the level of streptomycin in the fetal blood reaches one-half that in the maternal bloodstream, there have as yet been no comprehensive studies regarding the concentration of *p*-aminosalicylic acid and isoniazid in the fetal blood when administered in therapeutic doses to tuberculous pregnant women. Amaya-Leon (*Rev. colomb. obst. y ginec.* **5**:5, 1953) has reported on a series of 16 pregnant women treated with isoniazid. No adverse effect on the fetus was noted in any instance. Ravina and co-workers (*Ann. méd.* **53**:770, 1952) report the case of a pregnant woman suffering from miliary tuberculosis who received therapy for five months with isoniazid. At the end of this time she gave birth to a normal child, and the level of isoniazid in the child's cord blood was virtually that of the mother's blood examined at the same time.

IMPOTENCE AFTER CASTRATION

To the Editor:—*A 22-year-old man complains of impotence. Past history revealed bilateral undescended testes. His development otherwise had been normal, and he had had satisfactory sexual intercourse on numerous occasions. Last April he had pain in both groins and saw another physician. An operation was performed, and the surgeon removed both testes because they could not be brought down into the scrotum and because the incidence of cancer is increased in cryptorchism. In July, this year, the patient married and since then has been unable to gain an erection, although he had them after surgery. There is no history of injury to the spinal cord, brain, etc. Physical examination was normal. I felt that the impotence was on a psychological basis and explained the whole thing to the patient. I also felt he should be getting supplementary male hormone. Is this necessary, or will the adrenals take over? I would like information about dosage.*

M.D., Minnesota.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—The androgen component of the adrenal cortex is not capable of supplanting that needed in the castrated male. It is suggested that the patient described above be started with injections of testosterone propionate, 50 mg. given intramuscularly, three times weekly for at least three weeks, after which time dosage can be reduced and regulated to suit this particular patient's requirements. Once the weekly requirement is ascertained, other routes of administration may be calculated. Orally, three to four times the amount is required to obtain the same result as with injected testosterone. Two 75 mg. pellets of testosterone is equivalent to 25 mg. of testosterone propionate; therefore, for each 25 mg. of testosterone propionate required weekly, two pellets should be implanted.

Answer.—The impotence, at this time, is probably on a psychological basis. Eunuchs are often potent immediately after castration, but the potency gradually decreases if no supplemental therapy is introduced. This patient would probably be benefited by testosterone propionate in oil, 25 mg. intramuscu-

larly daily, then tapering off the dose according to the patient's needs. Testosterone propionate tablets for sublingual use, 25 mg. daily, may also be used. The subcutaneous implantation of testosterone propionate, 100 mg. in beeswax, may be attempted, but intramuscular or sublingual medication is probably indicated first. It is noted that this patient was castrated because the surgeon was concerned about the incidence of cancer in cryptorchism. If the undescended testis cannot be brought down into the scrotum, it is best left in the abdominal position, because of the internal secretion of the testis. While it is true that malignant change is commoner in the undescended than in the descended testis, the incidence of cancer in the undescended testis is not great enough to consider the undescended testis to be a precancerous lesion. The incidence of malignant disease in undescended testis is about 2 to 4%. When one considers that the incidence of malignant disease in the normal breast is about 2%, one may say too much emphasis has been given the danger of cancer in cryptorchism. Also, bringing the undescended testis into the scrotum does not decrease its liability to malignant disease.

GLUCOSE TOLERANCE TESTS ON EXECUTIVES

To the Editor:—*We are doing physical examinations on a group of executives who come into the hospital for three days and are given a thorough "going over." Among other things, a three hour glucose tolerance test (fasting blood sugar level, administration of 100 gm. of glucose, and blood sugar level determinations at one, two, and three hour intervals) is given. We have had a number of low values, not infrequently below 60 mg. per 100 cc.; a few values in the low 40's; and quite a number of flat curves with a maximum variation of less than 20 mg. per 100 cc. We have had also a number of higher-than-normal curves with two hour blood sugar values above 120 mg. per 100 cc., which by our technique is considered the maximum normal value. Some of the lower curves and some of the higher curves have been rechecked at a later date and have been found to be normal. Although laboratory errors are to be ruled out, other factors might have an effect on the metabolism of glucose, and it is about these we would like an opinion. The glucose tolerance tests are done on the third day of hospitalization. For three days prior to this the men receive purgatives each evening, and they have no breakfast for the three mornings preceding the tests. One of the evening meals is a low-fat meal in preparation for cholecystography.*

How much influence on the glucose tolerance test might we expect from alteration in intestinal function due to the purgings? How much change in islet function and other metabolic factors related to the metabolism of glucose might be anticipated from the three days of somewhat inadequate diet? What bearing would the patient's prior nutritional status have? Would you consider the test as we perform it adequate as a screening test for diabetes, and, if not, what modifications would you suggest? Would you consider screening for hypoglycemia warranted, and, if so, would the type of test under discussion be adequate? *Harry L. Hunter, M.D., Chicago.*

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.— Under no condition would the glucose tolerance test as now planned following three days of purgings and three mornings without breakfast be considered reliable. It is easy to get abnormal glucose tolerance tests unless the patient is on a full diet for several days before the test is performed. A two hour glucose tolerance test should suffice, and a decision as to the presence of diabetes would depend on the whole curve: on whether the fasting blood sugar is below 130 mg. per 100 cc., the peak under 170 mg. per 100 cc., and the two hour level about the same as the fasting or lower, although even if it happened to be 125 mg. per 100 cc. it should not be considered positive.

Here are a few suggestions. One could have the patient arrive at 5 p. m. without having had anything to eat or drink, save water, since 1 p. m. the same day. At 6 p. m., which would be five hours after the last meal, he would be given 100 gm. of glucose and the test carried out for two hours. Following that, the regular procedures incidental to the study could be begun. A second method would be to determine the blood sugar level on arrival and to give 50 gm. of glucose with the evening meal and, one hour afterward, repeat the blood sugar determination. According to the result one could decide whether a further test was necessary. The most reliable method of all would be to have the 100 gm. glucose tolerance test for two hours done fasting the morning after arrival. All kinds of variations in blood sugar levels will be found in doing routine glucose tolerance tests, but one sees very few blood sugar levels as low as 40 mg. per 100 cc.

Answer.—1. It is to be expected that in a rather large series of glucose tolerance curves a certain number of diabetics will be discovered, particularly in the age group of executives. It is also to be expected that some normal persons will have flat curves on at least one test. I take it, however, that the deviations from normal are more frequent than would be expected. If this is true, then the questions asked are pertinent. 2. It would be much better if the tests were done on the first day of hospitalization, before intestinal purgings and restrictions of carbohydrate intake have been instituted. Both of these procedures would be expected to produce some lowering of liver glycogen and possibly some interference with the absorption of carbohydrate. Furthermore, it is well known that a period of restricted carbohydrate intake for several days (it is not certain whether three days is sufficient) will result in a mildly diabetic type of glucose tolerance curve in an otherwise normal person. 3. The glucose tolerance test as now being performed is the best screening test for diabetes available. 4. Hypoglycemia of a significant degree is relatively uncommon and would not justify a routine screening test. If the glucose tolerance test were prolonged to five hours, this would no doubt detect some cases of hypoglycemia that would be otherwise unsuspected. It is doubtful that the five hour test would be worth while as a routine procedure, however.

IODIZED SALT

To the Editor:—*What are the indications for iodized salt in a territory where there is very little goiter? I find that most patients use iodized salt routinely. In this area there seems to be a great deal of hypothyroidism, and I wonder if the use of iodized salt has any bearing on the matter.*

Joseph G. Wilson, M.D., Moscow, Idaho.

Answer.—Iodized salt is indicated to supplement an insufficient supply of iodine for the prevention of simple or endemic goiter. If the natural intake of iodine from foods and water is too low there is an increase in the incidence of simple goiter, particularly at puberty, during and after menopause, and during pregnancy. Goiter in domestic animals also occurs in such districts or regions. The need for an iodine supplement is present in all communities where a survey of the school population reveals a 10% incidence of thyroid enlargement in girls between the ages of 10 and 16 years.

For more than 125 years the danger of giving supplementary iodine has been studied both in planned and in natural experiments. No injurious effects have been detected. Crude salt is the most widely distributed natural source and also the simplest means of administering these traces of iodine. When these traces of iodine are removed by modern methods of refining salt, artificially added iodine becomes the simplest and cheapest way of handling this public health problem. There is no evidence that hypothyroidism is induced by an iodine supplement. This has been and is being demonstrated daily in many regions of the world, notably Switzerland. The Japanese also have for centuries used seaweed (which contains large quantities of iodine) as food, and as a consequence both simple goiter and toxic diffuse goiter are extremely rare among them.

Hypothyroidism is a rather indefinite term, and such a diagnosis is usually arrived at by a metabolic rate determination. It should always be borne in mind that depression of the metabolic rate alone is insufficient proof of true hypothyroidism. Thyroid cells, depressed to endothelial flatness for years, have been

known to promptly respond to stimulation, as indicated by the change from flattened to high columnar cells. Hence it is most improbable that the depression of thyroid functional activity resulting from adequate iodine intake (thyroid hormone production) could lead to true hypothyroidism. Iodine administration depresses the functional activity of the thyroid gland indirectly by decreasing the output of thyrotropic hormone of the anterior pituitary, which is the only known activator of the thyroid gland.

PRECAUTIONS AGAINST INFECTIONS IN HOSPITALS

To the Editor:—*In* The Journal *of Oct. 9, 1954, page 669, is a query concerning infectious precautions considered necessary in a hospital. I would suggest that acute viral hepatitis be added to the list of diseases requiring special precautions against transmitting the infection from the hospitalized patient. Foremost should be "stool precautions" not unlike typhoid precautions. Individual thermometers should be assigned to each patient for his exclusive use, and the thermometer should be destroyed on the patient's discharge. This should certainly apply without question to the rectal taking of temperatures and probably is indicated in the oral taking of temperatures. In addition to the precautions already listed in the reply to this question, one should add, for this disease, utmost care on the part of nursing, medical, and technical personnel not to inject oneself with the patient's serum. These precautions would apply to both the infectious hepatitis (or virus A) and the serum hepatitis (or virus B) varieties, even though in the latter variety stool precautions would not be required. However, since one can rarely be absolutely certain that a case is caused by one variety and not the other, it is safest to adopt all precautions against the transmission of these viruses that are based on present knowledge of the epidemiology of this disease.*

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ANTICOAGULANTS FOR TESTS

To the Editor:—*In* The Journal *of Jan. 15, 1955, page 304, there is a query about anticoagulants that can be used for hematological purposes as well as for blood sugar, urea nitrogen, and nonprotein nitrogen level determinations. The consultant advises the use of ammonium and potassium oxalate. While this is the anticoagulant of choice for hematological purposes, it should not be used for urea nitrogen or nonprotein nitrogen determinations. Most methods for these procedures are based on a color change occurring by the action of Nessler's solution (aqueous solution of 5% potassium iodide, 2.5% mercuric chloride, and 16% potassium hydroxide) and ammonia. It is common experience that the ammonium oxalate used as the anticoagulant will, therefore, lead to abnormally high values of urea nitrogen and nonprotein nitrogen. If a laboratory insists on using only one anticoagulant, the anticoagulant of choice should be heparin.*

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To the Editor:—*In the query "Anticoagulants for Tests" in* The Journal *of Jan. 15, 1955, page 304, a physician inquires about anticoagulants for the performance of various hematological tests as well as determination of blood sugar, blood urea, and nonprotein nitrogen levels. The answer as published is incorrect. The double oxalate recommended by the consultant cannot be used for the determination of blood urea or nonprotein nitrogen levels because of the ammonium. Should it be used as advised, the inquirer would obtain an alarmingly large number of apparent renal dysfunctions and threatened uremias. For the determination of blood urea and nonprotein nitrogen in a small laboratory only potassium oxalate should be used as the anticoagulant in a concentration of 2 mg. per cubic centimeter (0.1 cc. of 20% solution for 10 cc. of blood). The double oxalate should be used only for hematological tests.*

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To the Editor:—*In the query in* The Journal *for Jan. 15, 1955, page 304, regarding a suitable anticoagulant for venous blood samples, the inquiring physician stated he would like to perform either the blood urea or the nonprotein nitrogen determination on the blood sample. If the anticoagulant recommended in the reply is used, it would be impossible to determine the nonprotein nitrogen level by the usual laboratory methods, since the anticoagulant contains ammonium and the test itself is based on the formation of ammonia. It would still be possible to determine the blood urea level if an allowance is made for the ammonium content, but this would require two determinations. However, if potassium oxalate alone were used, the resultant shrinkage of erythrocytes would interfere with the hemogram and sedimentation rate. Although more expensive, heparin would be suitable as an anticoagulant, allowing 2 mg. of heparin for each 3 cc. of blood; this amount can be calibrated as a capillary drop if 150 mg. of heparin is dissolved in 2 cc. of distilled water and the capillary pipette is adjusted to deliver 75 drops per cubic centimeter.*

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To the Editor:—*I am referring to the query from Dr. J. F. Noguera of Praco, Ala., on page 304 of* The Journal, *Jan. 15, 1955, regarding a universal anticoagulant suitable for use in hematological and chemical procedures. The ammonium potassium oxalate (Heller-Paul) solution that you have indicated is probably ideal for hematology, but the presence of the ammonium radical in this solution precludes its use in the determination of blood nonprotein nitrogen levels or for any procedure in which a Kjeldahl determination with nesslerization is carried out. In this laboratory we use a 40% potassium fluoride solution (2 drops per 10 cc. of blood) as an anticoagulant for routine chemical studies in addition to the Heller-Paul solution for hematological procedures. We feel that it is better to use two anticoagulants than to sacrifice the advantages of each; the Heller-Paul solution is used for maximal preservation of cells and potassium fluoride for preservation of chemical constituents and the inactivation of enzymes.*

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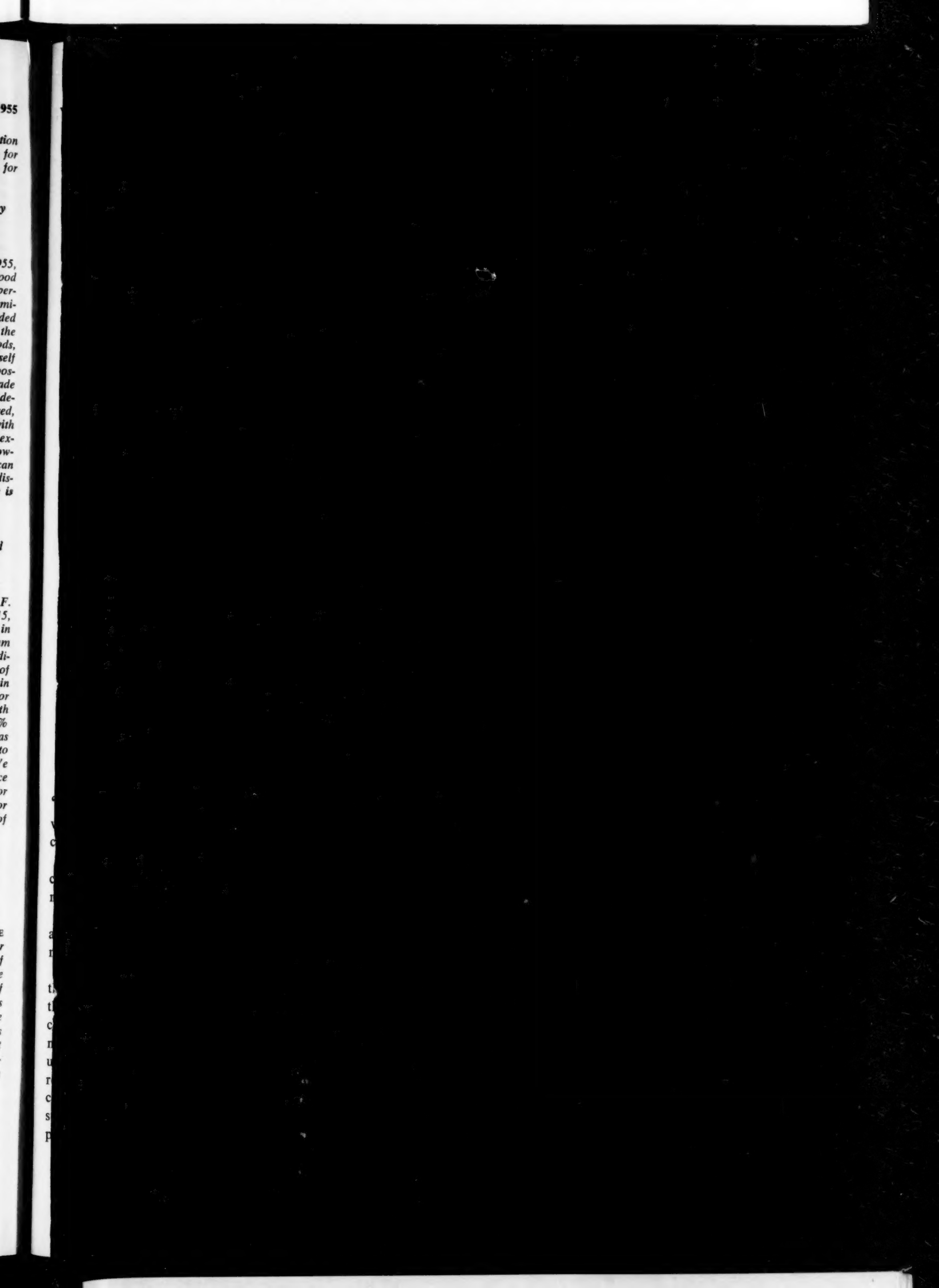
To the Editor:—*Regarding a query on page 304 of* The Journal *for Jan. 15, 1955, on an anticoagulant suitable for various laboratory determinations, may I suggest the use of the sodium salt of ethylenediaminetetraacetic acid (Versene sodium or Sequestrene sodium). This product has proved of exceptional value in our laboratories. We have found this anticoagulant to preserve the chemical constituents of the blood as well as the cellular elements for much longer periods than either of the oxalates, singly or in pairs. Also permit me to question the use of an anticoagulant containing ammonium ions, since their presence will give erroneously high results in urea and nonprotein nitrogen determinations.*

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